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American Journal of Diseases of Children

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# GROWTH OF THE THYMUS

## ITS RELATION TO STATUS THYMICOLYMPHATICUS AND THYMIC SYMPTOMS *

EDITH BOYD, M.D.

MINNEAPOLIS

The thymus gland has been described as either the sole cause or an associated cause of several pathologic conditions. Each concept advanced as to its origin, function, growth and pathologic significance has immediately been challenged. The result in the literature is chaos. In general, the studies on the thymus can be divided into three main groups: first, its mechanical effects; second, its significance in lymphatism, and, third, its growth and involution.

Under the mechanical effects, Plater (1614), according to Ruhräh's "Pediatrics of the Past," was the first to describe a death, "mors thymica," caused by suffocation from pressure made on the trachea by the thymus. His description reads like many necropsy records of the present time in which death is ascribed to status thymicolymphaticus. The anatomic relations given by Plater [1] are those found in all infants.

In this group belong also the clinical pictures attributed to the pressure of a "persistent" or "enlarged" thymus. During the first year of life, usually beginning at about the age of 1 month, a certain num-

* Received for publication, Dec. 31, 1926.

* From the Departments of Pediatrics, Pathology and Anatomy at the University of Minnesota Medical School. Read before the Colorado State Medical Society, Sept. 23, 1926.

1. Plater, F.: Observationum in hominis affectibus plerisque,—libri tres, Basileae, 1614, p. 172, quoted by Ruhräh, John: Pediatrics of the Past, ed. 1, New York, Paul B. Hoeber Inc., 1925, p. 239. ("Suffocation from a hidden internal struma, about the throat. The son of Marcus Peresius, five months of age, well nourished, with no previous illness, suddenly died from difficult breathing, suffocation. As the father had previously lost two sons from the same malady and being desirous of knowing the cause, we opened the chest, at his request. We found the gland in the region of the throat as a large protruding tumor, one ounce in weight, spongy, fleshy and pendant, replete with veins, adherent by membranes to the largest ascending vessels adjacent to the throat; these being filled with blood and flowing into the struma, dilated it to such an extent that it compressed the blood vessels in the locality; in which manner I concluded the child was thus suffocated.")

ber of infants have one or more of the following symptoms:[2] paroxysmal cough, dry and hacking nocturnal cough, intermittent inspiratory stridor, continuous or remittent dyspnea, choking while nursing, spells of cyanosis, and retraction of the head. All these symptoms, especially fussing and choking, are frequently relieved by lying on the side with the head back or with the head hanging, and are intensified by flexing the head on the chest. There has been considerable controversy on the relation of the width of the thymic shadow on a roentgen-ray film to thymic symptoms, at what point the shadow is that of an enlarged thymus, and whether to treat the child with the roentgen ray according to the symptoms or the width of the shadow.[3]

The group of mechanical effects should not be confused with status thymicolymphaticus, first described by Paltauf,[4] who considered prominent lymphoid tissue and thymus as anatomic evidence of a constitutional weakness, "anomele Körperconstitution." In such cases the patient is so constituted that he is killed by insignificant causes, as compared to those necessary to bring about the death of a normal person. In examining the reports of Paltauf's five cases, I find that he has not recorded the thymus weights, but that the dimensions given are within the normal limits established by von Sury.[5] The aorta was narrowed

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2. Friedlander, A.: Enlargement of the Thymus Treated by Roentgen Ray, Am. J. Dis. Child. **14**:40 (July) 1917; Blackfan, K. D., and Little, K.: A Clinical and Radiographic Study of the Thymus in Infants, Am. J. Dis. Child. **22**:459 (Nov.) 1921; Freeman, R. C.: The Symptoms and Treatment of Thymus Hypertrophy in Infancy, Arch. Pediat. **40**:665, 1923; Pfahler, G. E.: The Diagnosis of Enlarged Thymus by the X-ray and Treatment by X-ray or Radium, Arch. Pediat. **41**:39, 1924; Bliss, G. L.: A Study of Thymus Glands, Arch. Pediat. **42**:213, 1925. (Bliss suggests the term "symptom-producing thymus gland.")

3. Gerstenberger, H. J.: The Factor of Position of Diaphragm in Roentgen-ray Diagnosis of Enlarged Thymus, Am. J. Dis. Child. **21**:534 (June) 1921. Liss, I. E.: The Thymic Shadow in Infants, Am. J. Dis. Child. **24**:192 (Sept.) 1922. DeBuys, L. R. and Samuel, E. C.: A Study of Shadows in the Thorax of the Newly Born, Am. J. Dis. Child. **24**:397 (Nov.) 1922. Drea, W. F.: The Enlarged Thymus Gland, J. Radiol. **5**:193, 1924. Friedman, L. J.: X-ray Therapy of Chronic Cough in Children, Arch. Pediat. **42**:208, 1925; also footnote 2. Wasson, W. W.: Radiography of the Infant Chest, with Special Reference to the "Progression of the Chest and the Determination of the Normal," Radiol. **5**:365, 1925.

4. Paltauf, A.: Ueber die Beziehung der Thymus zum plötzlichen Tod, Wien klin. Wchnschr. **3**:172, 1890; **2**:876, 1889.

5. Sury, K., von.: Ueber die fraglichen Beziehungen der sog. Mors thymica zu den plötzlichen Todesfällen im Kindesalter. Vrtljschr. f. gerichtl. Med. **36**:88, 1908. (The average dimensions of the thymus as established by von Sury were: for from 8 months to 2 years, length 7.5 cm.; breadth, 5.7 cm.; thickness, 1.4 cm., and for from 2 to 14 years, length, 9.7 cm., breadth, 6.1 cm., thickness, 1.3 cm. The dimensions given by Paltauf were: for the age of 17 months, length, 9.5 cm.; breadth, 6 to 5 cm.; thickness, 2.5 cm., and for patients from 20 to 28 years of age, lengths, 10 cm., 10 cm. 9 cm., 7 cm.; breadths, 5 to 6 cm., 6 to 8 cm., 6 cm., 5 cm.; thickness, 1 cm., 1 cm., 1.5 cm., 1.5 cm., respectively.)

in three cases,[6] and a comparable criterion was not given in describing the lymph nodes. This work seems hardly an adequate basis for a new pathologic entity; nevertheless, this concept of status thymicolymphaticus was accepted and given as the cause of death in any person with a thymus weighing more than 15 Gm. and with lymphoid tissue which, in the pathologist's opinion, was "enlarged." Paltauf described his subjects as pale, overweight, rachitic infants found dead, and as young, well-nourished adults who dropped dead while in swimming. In the literature, status lymphaticus is spoken of as a constitutional state of infancy, or as the normal infantile lymphoid status retained after puberty, with or without a narrowed aorta, or as a state occurring at any age.[7] The common feature in most cases is sudden death. However, Symmers [8] claims that it is possible to make the diagnosis from microscopic sections of lymph nodes, without regard to their size. Many of the accounts of death from status thymicolymphaticus would make excellent material for a Sunday magazine section.

In contrast to most studies on status lymphaticus, careful work has been done on the growth and involution of the thymus, especially by Hammar.[9] According to him,[10] there are four concepts of thymus growth in the literature: first, the thymus reaches its maximum size at birth and then atrophies; second, it reaches its maximum at birth, remains stationary for from one to two years and then atrophies; third, it increases from birth to puberty and then atrophies; fourth, the thymus entirely disappears sometime between the ages of 1 and 20. Hammar has demonstrated that the confusion regarding the normal size of the

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6. From the teaching files of R. E. Scammon of the Department of Anatomy, University of Minnesota. Comparison of the average circumference of the aorta as established by Scammon with those given by Paltauf for the corresponding ages: Scammon, 6.2 cm., 6.5 cm., 6.4 cm.; Paltauf, 4.0 cm., 4.0 cm., 3.5 cm.

7. Howland, J.: The Symptoms of Status Lymphaticus in Infants and Young Children, Tr. Am. Pediat. Soc. **19**:51, 1907. Thursfield, H.: Discussion on Status Lymphaticus, Section for Study of Disease in Children, Proc. Roy. Soc. Med., part 1, **7**:186, 1913-1914. MacCallum, W. G.: A Text-Book of Pathology, ed. 1, Philadelphia, W. B. Saunders Company, 1917, p. 781. Emerson, H.: Status Lymphaticus in Adults, Its Clinical Diagnosis and Importance, Arch. Int. Med. **13**:169 (Jan.) 1914. Warthin, A. S.: The Pathology of Thymic Hyperplasia and the Status Lymphaticus, Arch. Pediat. **26**:597, 1909.

8. Symmers, D.: Status Lymphaticus, Am. J. M. Sc. **156**:40, 1918.

9. Hammar, J. A.: Ueber Gewicht, Involution und Persistenz der Thymus in Postfötalleben des Menschen, Arch. f. Anat. u. Physiol., Anat. Abt., suppl. vol., 1906, p. 91: Methode, die Menge der Rinde und des Marks der Thymus, sowie die Anzahl und die Grösse der Hassallschen Körperzahlenmässig festzustellen, Ztschr. f. Ange. Anat. **1**:311, 1914; The New Views as to the Morphology of the Thymus Gland and their Bearing on the Problem of the Function of the Thymus, Endocrinol. **5**:543, 1921; Die Menschenthymus in Gesundheit und Krankheit, Ztschr. f. mikr.-anat. Forschung, 1926, vol. 6. Hammar, J. A.: Fünfzig Jahre Thymusforschung, Ergebn. d. Anat. u. Entwcklngsgesch. **19**:1, 1909.

10. Hammar, J. A.: Arch. f. Anat. u. Physiol., Anat. Abt., suppl. vol., 1906, p. 91.

gland is caused by failure to recognize the occurrence of age involution, beginning at puberty, and "accidental involution," occurring in inanition or in any condition which causes loss of weight. By taking thymuses from patients who died of adequate pathologic cause within twenty-four hours of the onset of illness, he established new normal standards for thymic weight for given age groups. Beginning with an average weight of 13 Gm. at birth, the thymus increases to an average weight of 35 Gm. at puberty, then atrophies to 15 Gm. by the age of 50. Using the same criteria, Scammon has increased the number of cases to 1,074. Chart 1 shows the resulting growth curve of the thymus compared to that of the mesenteric lymph nodes. The two are parallel. Only the

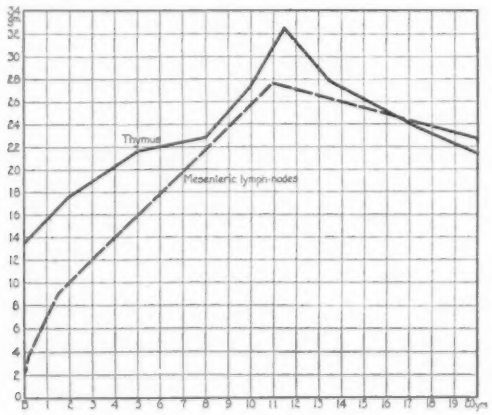


Chart 1.—Comparison of the growth curves of the thymus and of the mesenteric lymph nodes. (By courtesy of Dr. R. E. Scammon, Department of Anatomy, University of Minnesota.)

lymphoid tissue and the thymus have this type of postnatal growth curve. Therefore, as far as weight is concerned, the thymus acts as a lymphoid organ.

According to Hammar,[11] the microscopic changes of age involution consist of a loss of lymphocytes, changes in the reticular cells and infiltration of fat and connective tissue. Those of accidental involution, which occur at any age, are the same, except for the absence of infiltration of fat and connective tissue. The latter form of involution has been demonstrated experimentally in chronic and in acute inanition in rats.[12] Jonson [13] found a reduction of about 80 per cent in the cortex

11. Hammar, J. A.: Endocrinol. **5**:43, 1921.
12. Jackson, C. M.: The Effects of Inanition and Malnutrition upon Growth and Structure, ed. 1, Philadelphia, P. Blakiston's Son & Company, 1925, p. 285.
13. Jonson, A.: Studien über die Thymusinvolution. Die Akzidentelle Involution bei Hunger, Arch. f. mikr.-anat. **73**:390, 1909.

of these animals after four days of acute inanition. Hammar [11] notes another interesting point, that, in diseases such as influenza, there is an involution similar to that of inanition, even though the body is still well nourished. Experimentally, the roentgen ray [14] causes a reduction of lymphocytes in the cortex, thus decreasing the size of the gland.

We may now consider, first, whether the thymus produces death or symptoms mechanically, and second, whether Hammar's evidence on the growth and involution of the thymus clarifies the concepts of status lymphaticus.

## MECHANICAL EFFECTS OF THE THYMUS

In my necropsy records since 1915, there has not been a single case in which pressure on the trachea by the thymus could be interpreted as the cause of death. But, both in these records and in the literature, a thymus weighing more than 20 Gm. has been taken as evidence of death from suffocation or as evidence of the lymphatic state, without adequate dissection to prove or disprove mechanical compression of the trachea. Hence there is not reliable data to substantiate the diagnosis of "mors thymica." It is anatomically a possibility.[15]

In explaining the mechanical production of symptoms by the thymus it is necessary to have in mind the following points: (1) the normal increase in size of the structure, as shown in chart 1; (2) changes in shape and position during the first two weeks of life, due to expansion of the lungs; (3) the transient loss of thymic weight during the first weeks of life; (4) the rapid rate of growth of the chest as compared with the growth of the thymus in infancy.

The variability in size and shape of the thymus has long been recognized. Coplin [16] described the gland as unilobar, bilobar, trilobar and

14. Hammar, J. A. (footnote 11). Jackson, C. M. (footnote 12).

15. Noback, G. J.: A Contribution to the Topographic Anatomy of the Thymus Gland, with Particular Reference to its Changes at Birth and in the Period of the New-Born, Am. J. Dis. Child. **22**:120 (Aug.) 1921. ("The thymus in late fetal life and in the newborn is related posteriorly to the pericardium over the base of the heart and great vessels. On the left it may extend, in exceptional instances, as in one of this series, to the left vagus nerve. On the right it is generally found to be applied closely to the superior vena cava. The left innominate vein, and, occasionally, the superior vena cava, is embedded in the posterior aspect of the thymus. In a few cases it was found that these vessels actually ran through the substance of the gland. The innominate artery is closely applied to the trachea and crosses it diagonally, and the left innominate vein passes across the artery at the level of the upper border of the sternum. An increase in the anterior-posterior extent of the thymus in this region would, due to the rigidity of the superior thoracic aperture, compress the above named structures. In several of my cases this had evidently occurred. In these specimens the innominate artery was so greatly compressed against the trachea that it left a definite furrow marking its course across this tube thus markedly reducing the lumen.")

16. Coplin, W. M. L.: Morphology of the Human Thymus, Publ. Jefferson Medical College and Hospital **6**:116, 1915.

conglomerate. Noback [15] showed that the normal fetal thymus is broad and is changed to an elongated type by respiration. Figures 25 to 36, inclusive, of Noback's article show the transition from the fetal broad type to the infantile elongate type produced by the expansion of the new-born lungs. This process takes about two weeks following birth. Noback demonstrated, by transverse sections of the body, that the expanding lungs force the thymus posteriorly into the mediastinum and laterally and inferiorly around the heart, so that parts of the gland may extend backward to the trachea and vertebral column and downward to the diaphragm.

In my cases of the first two weeks of life, I found a loss of weight in the thymus of from 5 to 8 Gm. from the mean birth weight of 13 Gm. By six weeks the weight averages 17 Gm. Since there are few deaths of well nourished children during the first month of life, the material is not adequate as yet to establish the age at which the thymus regains its birth weight. There is some evidence to show that this process parallels the normal loss in body weight and recovery within the first ten days to two weeks.

Putting these observations together gives the following process: During this period while the thymus in the new-born child is being compressed around and between the mediastinal structures, it is also losing weight. After this process is well under way or is complete, the gland begins to increase in size, so that the portions of the thymus around and between the blood vessels and the trachea may grow sufficiently to cause pressure on vessels and nerves, particularly on the recurrent laryngeal nerve. There are two clinical observations which support such a hypothesis: first, most children do not develop thymic symptoms until from 1 month to 6 weeks of age; second, these children frequently have, along with an inspiratory stridor, hoarseness and a crowing cry suggestive of spasm of the vocal cords from irritation of the recurrent laryngeal nerve. Blackfan [17] noted that this cry sounds like the brassy voice of a man with an aortic aneurysm.

If this mechanical explanation of "thymic" symptoms is true, roentgen-ray treatments are justified for reduction of the size of the thymus in children with symptoms, even though they are produced by a normal gland.[18] It is known that children with the clinical picture of so-called "thymic symptoms" are relieved by the roentgen ray or by radium applied to the upper mediastinum. It is assumed that this relief is due to reduction in size of the thymus, since reduction from radiation has been demonstrated experimentally.[12] However, it has not been proved that there are not some other structures affected by this therapy.

17. Blackfan (footnote 2).
18. Bliss (footnote 2).

Finally, thymic symptoms do not appear after the first year of life, for, although the thymus is increasing in size, the chest is growing at a much greater rate, so that the gland becomes relatively insignificant.

## RELATION OF THE NORMAL GROWTH AND INVOLUTION OF THE THYMUS TO STATUS THYMICOLYMPHATICUS

Hammar's concepts of thymic growth, age involution and accidental involution may now be applied to the so-called thymic state, status thymicus, lymphatism, status thymicolymphaticus or lymphatic constitution.

Interest in this subject in the department of pathology of the University of Minnesota Medical School was first aroused by our own mistakes. Dr. E. T. Bell made the diagnosis of status lymphaticus in a child who was found in convulsions on a stairway, and who died a few minutes later. The following day a plumber, while climbing the same stairway, was rendered temporarily unconscious by an electric shock. One of the metal cleats on the stairway was loose, and, in slipping back and forth, made contact with the electric wires, thus completing a circuit carrying the full city current.

In another instance I was consulted on a coroner's case of a 5 year old boy who had died in convulsions ten minutes after the onset. I found nothing to account for the death. The lymphoid tissue was prominent, and the thymus weighed 50 Gm. The microscopic sections showed prominent lymph nodules in the lungs and in the spleen. I could find no evidence of infection, and finally committed myself by saying that this was the anatomic picture of status thymicolymphaticus. Since it was a coroner's case, I brought the contents of the stomach to the state toxicologist. Two months later I was called to testify in a murder trial for strychnine poisoning, about 25 mg. of strychnine having been recovered from this boy's stomach. From these and similar cases, in which there was early pneumonia, I became skeptical of the diagnosis of status thymicolymphaticus.

I have abstracted from the pathologic records of the last two years in this department all the necropsies on children over 2 weeks and under 15 years of age. In this series of 324 necropsies, the weight of the thymus was recorded in only 147, or 45.5 per cent. This selection is due to failure to weigh the thymus as a matter of routine in children after the first few months of life, especially if it is not prominent enough to attract the pathologist's attention or if he has found an adequate cause of death. I tabulated the thymus weights from the data according to nutritional ranking and body length. The nutritional rankings were made according to the thickness of the subcutaneous fat over the anterior abdominal wall and the pathologist's note on the body nutrition, using the common pathologic nomenclature as follows: very well nourished

++++; well nourished or good nutrition +++; moderately well nourished ++; poorly nourished +; emaciated —. The total body lengths were grouped by intervals of 10 cm. The results are shown graphically in chart 2. It is evident that, although there is increase in thymus weight with increase in body length, the mean weight of the thymus is much greater for all lengths in the ++++ and +++ classes than in ++, + and —. There is accidental involution superimposed on normal growth of the thymus in the last three groups.

Since the thymus weights fall into two main classes, I combined the cases of ++++ and +++ as "well nourished," and of ++, + and — as "poorly nourished." Using age instead of length,

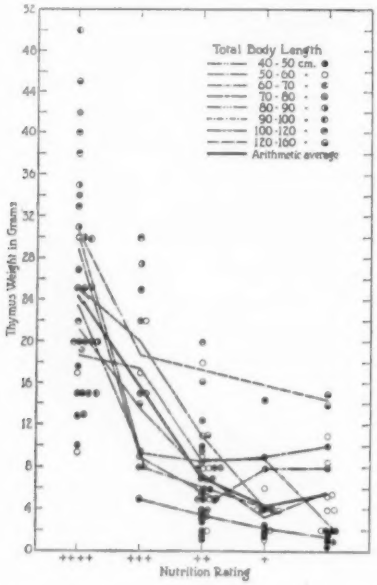


Chart 2.—Decrease of the thymus weight in children of known length with the lowering of nutritional status.

since most of the references did not give the length of the body, I arranged the thymus weights in my cases and in those from the literature according to this nutritional rating.[19] In the "well nourished" groups I found that Hammar's,[20] von Sury's,[5] Bratton's[21] and my data followed the same general curve, similar to Scammon's normal growth

19. From the German data, "sehr gut" and "sehr kraftig" were rated as ++++, "gut" as +++, "mässig" as ++, "mager" and "schmächtig" as + and —, except three cases in Hammar's data called "mässig," which were rated +++.

20. Hammar, J. A.: Ztschr. f. ange. Anat. **1**:311, 1914.

21. Bratton, A. B.: The Normal Weight of the Human Thymus, J. Path. & Bacteriol. **28**:609, 1925.

TABLE 1.—*Weight of Thymus (Gm.) in Well Nourished Subjects; Data from Various Sources (Number of Cases in Parentheses)*

| Source of Data | N.B. | 0-1 Mo. | 1-2 Mo. | 2-3 Mo. | 3-4 Mo. | 4-5 Mo. | 5-6 Mo. | 6-12 Mo. | 1-2 Yr. | 2-4 Yr. | 4-6 Yr. | 6-8 Yr. | 8-10 Yr. | 10-12 Yr. | 12-14 Yr. | 14-16 Yr. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hammar..... | 12.6 | 12.6 | 16.0 | 16.5 | 33.0 | .... | .... | 19.0 | 36.0 | 26.6 | .... | 20.0 | 25.8 | .... | 40.1 | 33.2 |
| (45 cases) | (21) | (3) | (1) | (1) | (1) | .... | .... | (1) | (2) | (5) | .... | (1) | (2) | .... | (1) | (6) |
| Von Sury.... | 13.7 | 14.1 | 20.3 | 22.9 | 26.9 | 22.9 | 19.0 | 24.8 | 19.6 | 14.5 | 22.5 | 29.0 | 34.5 | 32.2 | .... | .... |
| (97 cases) | (21) | (19) | (7) | (6) | (5) | (4) | (4) | (10) | (7) | (3) | (3) | (4) | (1) | (3) | .... | .... |
| University of Minnesota... | 13.5 | 9.6 | 15.5 | 22.3 | 21.9 | 5.0 | 18.4 | 19.3 | 20.1 | 19.4 | 28.6 | 15.0 | 27.4 | 25.0 | 45.0 | .... |
| (72 cases) | (13) | (3) | (4) | (4) | (4) | (1) | (5) | (9) | (10) | (6) | (9) | (1) | (1) | (1) | (1) | .... |
| Combination of foregoing 214 cases..... | 13.0 | 13.3 | 18.4 | 22.1 | 25.5 | 19.3 | 18.6 | 22.0 | 21.6 | 21.0 | 27.1 | 25.2 | 28.3 | 30.4 | 42.6 | 33.2 |
| | (55) | (25) | (12) | (11) | (10) | (5) | (9) | (20) | (19) | (14) | (12) | (6) | (4) | (4) | (2) | (6) |
| Bratton..... | .... | .... | .... | .... | .... | .... | .... | 22.1 | 26.0 | 26.1 | 23.9 | 30.0 | 27.9 | 29.4 | 25.0 | 27.5 |
| (247 cases) | .... | .... | .... | .... | .... | .... | .... | (13) | (27) | (60) | (47) | (30) | (26) | (17) | (12) | (15) |
| Combination of foregoing 461 cases..... | 13.0 | 13.3 | 18.4 | 22.1 | 25.5 | 19.3 | 18.6 | 22.0 | 24.2 | 25.1 | 24.6 | 29.2 | 27.9 | 29.6 | 27.5 | 29.2 |
| | (55) | (25) | (12) | (11) | (10) | (5) | (9) | (33) | (46) | (74) | (59) | (36) | (30) | (21) | (14) | (21) |

TABLE 2.—*Weight of Thymus (Gm.) in Well Nourished Subjects from the Data of Friedleben and von Mettenheimer*

| Source of Data | N.B. | 0-1 Mo. | 1-2 Mo. | 2-3 Mo. | 3-4 Mo. | 4-5 Mo. | 5-6 Mo. | 6-12 Mo. | 1-2 Yr. | 2-4 Yr. | 4-6 Yr. | 6-8 Yr. | 8-10 Yr. | 10-12 Yr. | 12-14 Yr. | 14-16 Yr. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Friedleben... | .... | 14.0 | 31.4 | 13.4 | 17.6 | .... | .... | 18.2 | 12.9 | 14.4 | 7.7 | .... | 8.5 | 19.9 | .... | .... |
| 26 cases | .... | (1) | (1) | (2) | (2) | .... | .... | (6) | (7) | (4) | (1) | .... | (1) | (1) | .... | .... |
| Von Mettenheimer | .... | .... | .... | .... | .... | 13.9 | .... | 11.4 | 10.2 | 13.7 | 10.1 | 10.2 | 10.3 | .... | .... | .... |
| 31 cases | .... | .... | .... | .... | .... | (1) | .... | (5) | (10) | (8) | (4) | (2) | (1) | .... | .... | .... |
| Combined data of foregoing 57 cases | .... | 14.0 | 31.4 | 13.4 | 17.6 | 13.9 | .... | 15.1 | 11.0 | 14.0 | 9.6 | 10.2 | 9.4 | 19.9 | .... | .... |
| | .... | (1) | (1) | (2) | (2) | (1) | .... | (11) | (17) | (12) | (5) | (2) | (2) | (1) | .... | .... |

TABLE 3.—*Weight of Thymus (Gm.) in Well Nourished Subjects from the Data of Nicoll and Bovard*

| Source | N. B. | 0-1 Mo. | 1-2 Mo. | 2-3 Mo. | 3-4 Mo. | 4-5 Mo. | 5-6 Mo. | 6-12 Mo. | 1-2 Yr. | 2-4 Yr. | 4-6 Yr. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Nicoll and Bovard. | .... | 7.5 | .... | 20.3 | 8.9 | 6.3 | 7.6 | 9.0 | 10.0 | 8.0 | 11.3 |
| (99 cases) | .... | (2) | .... | (2) | (3) | (3) | (3) | (52) | (15) | (17) | (2) |

TABLE 4.—*Weight of Thymus (Gm.) in the Poorly Nourished Subjects from Data from Various Sources*

| Source of Data | N.B. | 0-1 Mo. | 1-2 Mo. | 2-3 Mo. | 3-4 Mo. | 4-5 Mo. | 5-6 Mo. | 6-12 Mo. | 1-2 Yr. | 2-4 Yr. | 4-6 Yr. | 6-8 Yr. | 8-10 Yr. | 10-12 Yr. | 12-14 Yr. | 14-16 Yr. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Von Sury.... | .... | 7.5 | 7.6 | 13.5 | 4.9 | 13.0 | 10.0 | 9.8 | 6.7 | 8.1 | .... | 22.1 | 14.3 | .... | .... | .... |
| (58 cases) | .... | (13) | (17) | (2) | (5) | (3) | (2) | (3) | (8) | (3) | .... | (1) | (1) | .... | .... | .... |
| University of Minnesota... | .... | 4.3 | 6.0 | 9.5 | 10.5 | 5.0 | 4.0 | 7.9 | 8.2 | 9.3 | 10.4 | .... | 14.5 | .... | .... | .... |
| (61 cases) | .... | (11) | (14) | (7) | (4) | (2) | (1) | (8) | (5) | (3) | (4) | .... | (2) | .... | .... | .... |
| Friedleben... | .... | 4.5 | 2.6 | 3.8 | 3.6 | 8.4 | 4.3 | 3.9 | 3.3 | 4.7 | 2.5 | 0 | .... | 5.8 | 9.5 | .... |
| (68 cases) | .... | (10) | (5) | (5) | (1) | (2) | (5) | (14) | (10) | (7) | (6) | (1) | .... | (1) | (1) | .... |
| Von Mettenheimer | 3.7 | .... | 3.3 | .... | .... | 3.5 | 5.5 | 4.6 | 8.0 | .... | 5.9 | .... | .... | .... | .... | .... |
| (16 cases) | .... | (3) | .... | (2) | .... | .... | (1) | (2) | (3) | (4) | .... | (1) | .... | .... | .... | .... |
| Nicoll and Bovard..... | 7.8 | 6.2 | 5.4 | 5.4 | 5.6 | 5.4 | 4.4 | 5.0 | 3.9 | 6.7 | 8.9 | .... | .... | .... | .... | .... |
| (356 cases) | (9) | (13) | (18) | (16) | (14) | (25) | (18) | (143) | (42) | (52) | (6) | .... | .... | .... | .... | .... |
| Combined sources..... | .... | 5.9 | 6.0 | 6.5 | 6.2 | 6.3 | 4.7 | 5.1 | 4.5 | 6.8 | 6.9 | 9.3 | 14.4 | 5.8 | 9.5 | .... |
| (559 cases) | .... | (59) | (54) | (32) | (24) | (32) | (27) | (170) | (68) | (60) | (16) | (3) | (3) | (1) | (1) | .... |

curve; that of von Mettenheimer's [22] and Friedleben's [23] data showed a temporary increase in weight and then a loss, and that Nicoll and Bovard's cases [24] showed a decrease in weight from birth. I have plotted all this material in chart 3. All the data which gave both body height and weight were checked by plotting with respect to Bardeen's [12] curve of the normal height-weight index. My cases and von Sury's fall closely around this normal height-weight index curve, while von Mettenheimer's fall consistently below it.

Nicoll and Bovard's data could not be checked for accuracy of nutritional rating, except by documentary evidence, because: 1. Accepting Paltauf's diagnosis, they took children who had been ill for at least several days. 2. It is possible that their concept of a well nourished infant at the New York Foundling Home in 1906 might be different from the present day concept. All cases in all the data which were recorded as

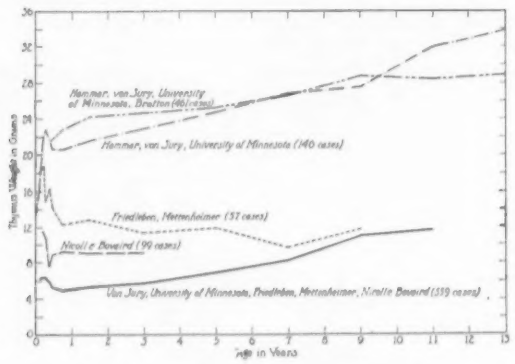
Hammar, von Sury, University of Minnesota, Bratton (460 cases)
Hammar, von Sury, University of Minnesota (140 cases)
Friedleben, Mettenheimer (57 cases)
Nicoll e Bovaird (99 cases)
Von Sury, University of Minnesota, Friedleben, Mettenheimer, Nicolle Bovaird (339 cases)
Thymus Weight in Grams
Age in Years

Chart 3.—Curves of thymus weight in childhood. Thymus weighs from well nourished children are indicated by broken lines, from poorly nourished children by a solid line (tables 1, 2, 3 and 4). The averages including Bratton's data were put in a separate curve because he did not give the diagnosis. (The curves were drawn from data after a single application of the three-point smoothing method.)

"poorly nourished" followed the same general weight curve, as shown by the solid line in chart 3. According to the upper curve for the well nourished, the average weight at birth is 13 Gm., at 6 months 20 Gm. and at 13 years 35 Gm. This curve probably shows the average weights of the thymus as found at necropsy in well nourished children. Von

22. Mettenheimer, H., von: Zum Verhalten der Thymusdrüse in Gesundheit und Krankheit, Jahrb. f. Kinderh. **46**:55, 1897.

23. Friedleben, A.: Die Physiologie der Thymusdrüse in Gesundheit und Krankheit, Frankfurt-am-Main Monograph, 1858. (Weights converted to metric system taken from 20.)

24. Nicoll, M., and Bovard, D.: The Weights of the Viscera in Infancy and Childhood, with Special Reference to the Weight of the Thymus Gland, Arch. Pediat. **23**:641, 1906.

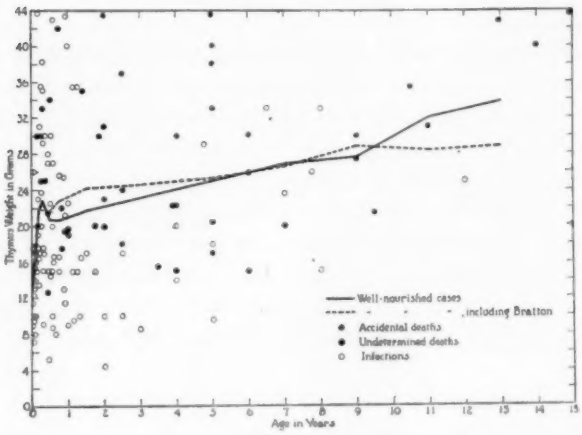


Chart 4.—Distribution of the thymus weights with respect to age and cause of death. The curves show the growth of the thymus in well nourished children, as shown in chart 3.

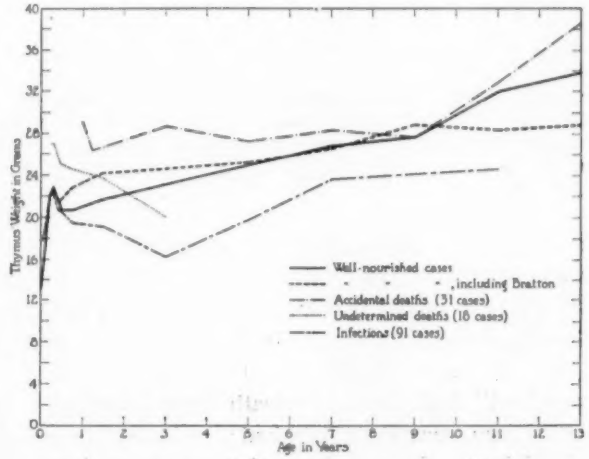


Chart 5.—Curves of thymus weights in childhood as determined from various categories of cases. (The curves were drawn from data after a single application of the three-point smoothing method.)

Mettenheimer [25] and Friedleben's curve represents a group of variable nutritional status, and Nicoll and Bovard's curve represents a fairly well nourished group.

I next divided all "well nourished" cases into (1) accidental deaths, in which the child had died from such factors as fracture of the skull, strychnine poisoning and carbon monoxide poisoning; (2) "undetermined deaths" and status lymphaticus; and (3) deaths from infections. The scattering of individual cases can be seen in chart 4. The curve of thymus weight in accidental deaths is the highest, the one for "undetermined deaths" intermediate, and the one for deaths from infection the lowest (chart 5). In other words, well nourished children killed by accidents have larger thymuses, for a given age group, than children who have supposedly died of lymphatism. The low thymus curve for deaths

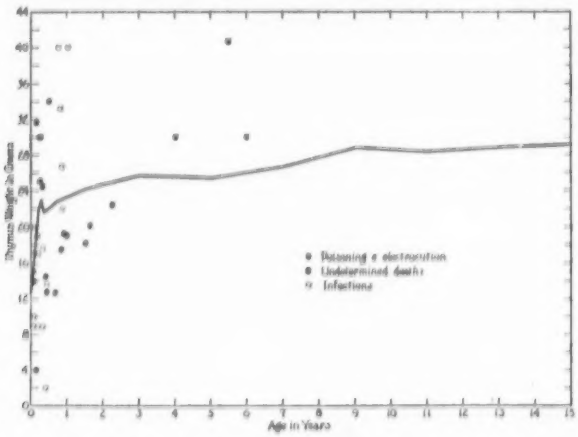


Chart 6.—Distribution of thymus weights obtained from necropsies of children who died suddenly (children found dead or dying within thirty minutes after the onset of symptoms). The cases were not selected according to nutrition. The curve is that of the mean thymus weight for well nourished children, including the data of Bratton.

from infection agrees with Hammar's observation of involution of the thymus in acute infections before the occurrence of loss of body weight.

As a final step, I plotted the cases of sudden death in which the child was found dead or died within one-half hour of the onset of illness, according to the following diagnoses: (1) poisoning and electrocution; (2) "undetermined" death, and (3) death from infections. In most of the cases the children were well nourished; the lowest three weights were in emaciated children. Chart 6 shows that thymus weights are not uni-

25. Von Mettenheimer recognized that his thymus weights were decreased. He considered this reduction due to the acute infectious diseases from which most of the children in his cases died.

formly high in children found dead. Obviously, there is not a high correlation between sudden death and thymus weight unless the child is well nourished.

The mesenteric lymph nodes seem to parallel changes in the size of the thymus, fluctuating as does the thymus with body weight. The most "prominent" nodes are seen in cases of accidental death. It has been demonstrated experimentally that the lymphoid tissue in rats decreases in size with inanition. So far, comparable quantitative criteria of the size of lymph nodes have not been generally used, so I have not attempted to classify them.

Routine microscopic examination shows the same stages of accidental involution as described by Hammar.[11] Nutrition and duration of illness can be estimated with a high degree of accuracy from the microscopic picture.

## SUMMARY

1. The thymus in the new-born child shows a temporary loss of weight which probably is concomitant with the normal loss in body weight.

2. The fetal type of thymus is broad, the infantile type elongate. This change in form is produced during the first two weeks of life by the expansion of the lungs (Noback).

3. Thymic symptoms may be produced during the first year of life by mechanical pressure of a normal gland on mediastinal structures, especially on the recurrent laryngeal nerve. My records do not show any case in which pressure on the trachea by the thymus caused death.

4. The anatomic picture that Paltauf described as that of status thymicolymphaticus represents the normal thymus and lymphoid tissue of the well nourished child.

5. Failure to recognize accidental involution has caused the confusion regarding thymus weight and the misconception, status thymicolymphaticus.

6. The average weight of the thymus found at necropsy in well nourished children is 13 Gm. at birth, 20 Gm. at 6 months and 35 Gm. at 13 years.

7. The average weight of the thymus found at necropsy in poorly nourished children is 8 Gm. at 2 weeks, 6 Gm. at 6 months and 13 Gm. at 13 years. In general, the fluctuations in the weight of the thymus at any age period are concomitant with fluctuations in body weight. Some illnesses, such as influenza, may affect the thymus before they affect body nutrition.

8. The growth curve of the thymus in a well nourished child is of the same type as that of the lymphoid tissues in general.

# ASTHMA IN CHILDREN

## III. THE INCIDENCE AND SIGNIFICANCE OF VARIOUS DISEASES AND INFECTIONS, AND OF TONSILLECTOMY AND ADENOIDECTOMY *

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In a previous study on the etiology of asthma,[1] the subject matter of this communication was scarcely touched on because it was considered of sufficient clinical importance to warrant special attention.

The rôle played by intercurrent infections and other diseases peculiar to childhood in initiating the onset or altering the course of asthma has been insufficiently considered until recently. Reference to the occurrence of asthma or "asthmatic bronchitis" as a possible complication or sequel of measles, pertussis, scarlet fever and other diseases of childhood or after tonsillectomy is rare in the standard textbooks on pediatrics. In the literature a few observations have been recorded which suggest a direct relationship between these diseases and asthma. Lucas [2] found a number of cases of asthma which gave a history of chronic bronchitis following pertussis. Licciardi [3] describes typical attacks of asthma occurring for the first time during measles. Kammerer [4] found that acute infectious conditions of the respiratory organs were often the determining factor in the first attack of asthma.

In this series the relationship between these infections and asthma was striking, and it is hoped that the observations recorded in this paper will lead toward a better understanding of the etiology and the numerous factors which influence the course of asthma.

The material of this paper was based on 100 consecutive cases of asthma in children ranging in age from 6 months to 14 years. All these subjects were under observation for from one to four years, the average being two and one-third years.[1]

### INFECTIOUS DISEASES

*Pertussis.*—Pertussis occurred in forty-three children of the allergic and in eight children of the nonallergic group,[5] a total incidence of 51 per cent.

* Received for publication, Dec. 31, 1926.

* From the Children's Asthma Clinic, Mt. Sinai Hospital.

1. Peshkin, M. M.: Asthma in Children. I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

2. Lucas, W. P.: Oxford Medicine, New York, Oxford Press, 1921.

3. Licciardi, S.: Di alcune nevrosi del Simpatico, ris contrate durante l'infenzione morbillosa, Gazz. d. osp. **30**:1353 (Oct. 26) 1909.

4. Kammerer, H.: Beziehung des Bronchialasthmas zu anderen Erkrankungen Die Bedentung akuter Infectionen der Respirationsårgane, München. med. Wchnschr. **69**:542, 1922.

5. In order to avoid confusion, the few cases of para-asthma (1) will be incorporated with those of the nonallergic group in this paper.

In seventeen cases of the allergic group and three of the nonallergic group there was a history of contracting pertussis prior to the onset of asthma. There was no relationship between the two diseases. Thirteen patients of the allergic group and three of the nonallergic group contracted pertussis after the onset of asthma. In most of these cases the asthma was aggravated during the course of pertussis and for some time after it.

In thirteen cases of the allergic group and in two cases of the nonallergic group a definite clinical relationship between pertussis and the onset of asthma was observed. In eleven of these cases the onset of asthma occurred during the course of or directly following pertussis. In the other four there was a definite history of "recurrent bronchitis and rhinitis" dating from the attack of pertussis to the onset of asthma, which occurred from six months to three and one-half years after the contraction of pertussis.

*Measles.*—Measles occurred in sixty-four children of the allergic group and in thirteen of the nonallergic group, a total incidence of 77 per cent.

Thirty-three patients of the allergic group and four of the nonallergic group had measles from several months to nine years prior to the onset of asthma, with no relationship between the two diseases. Twenty-seven patients of the allergic group and nine of the nonallergic group contracted measles after the onset of asthma. Asthma frequently recurred or was aggravated during the incubation period of measles, but with the appearance of fever the asthma cleared in the majority of these patients. The period of time these patients remained free from asthma varied from two weeks to three months.

In four cases of the allergic group and in none of the nonallergic group was there a definite clinical relationship between measles and the onset of asthma.

*Varicella.*—Chickenpox, although quite prevalent, was not observed to initiate the onset or to alter the course of asthma in a single case.

*Scarlet Fever.*—Scarlet fever occurred in seven cases of the allergic group and in one of the nonallergic group, a total incidence of 8 per cent.

In two cases of the allergic group and in one of the nonallergic group scarlet fever occurred prior to the onset of asthma, with no relationship between the two diseases.

Four patients of the allergic group contracted scarlet fever after the onset of asthma. All four were free from asthma at the time of the infection. One of these had a recurrence during convalescence; the other three were unaffected.

In one case of the allergic group and in one of the nonallergic group scarlet fever initiated the onset of asthma.

*Diphtheria.*—Diphtheria occurred in four children of the allergic group and in one of the nonallergic group after the onset of asthma, a total incidence of 5 per cent. All were treated with diphtheria antitoxin. Those who had asthma seemed to be benefited. This may have been partially due to the administration of antitoxin.

*Comment.*—The relative frequency with which pertussis and measles were found to be clinically associated with the onset of asthma was striking. Pertussis was responsible for initiating the onset of asthma in 15 per cent of the cases in this series, and measles in only 4 per cent. This is significant when it is considered that the incidence of measles in childhood is so much more frequent than that of pertussis. It would seem, therefore, that the influence of pertussis, particularly on the onset of asthma, should not be considered accidental.

The temporary beneficial effect of measles and diphtheria on the course of asthma may be attributed to the fever accompanying these infectious diseases. The anergic stage of measles also probably plays some rôle. This is in marked contrast to the unfavorable effect of pertussis on the course of asthma. It is of interest to note that pertussis in the absence of complications is usually an afebrile disease.

The association of pertussis, measles and scarlet fever with the onset of asthma in 22 per cent of the cases in this series is sufficiently striking to command attention, especially from the standpoint of prophylaxis. In most of these cases the etiologic factors in the onset of asthma were usually the inhalant proteins. If a child contracts pertussis, and there is an allergic family history, especially with an antecedent eczema, angioneurotic edema or "recurrent bronchitis and rhinitis," the elimination of the known sensitizing substances from the diet and environment may possibly prevent the onset of asthma.

### INFECTIONS OF THE UPPER RESPIRATORY TRACT

*Acute Rhinitis and Bronchitis.*—Acute rhinitis and bronchitis are the most common ailments of man, and up to recent years they were considered solely infective in origin. In the light of present knowledge recurrent rhinitis and bronchitis, particularly when unaccompanied by fever, are often manifestations of allergy and may be the forerunner of asthma. Infection of the upper respiratory tract superimposed on an allergic rhinitis or bronchitis adds greatly toward precipitating the onset of asthma. Such infections may also render a person with a predisposition to allergy sensitive to various protein substances.

It is conceded that allergic persons are frequently susceptible to upper respiratory infections. These infections are often held solely responsible for the asthmatic attack. It cannot always be determined with certainty whether a rhinitis or bronchitis is an infection or an allergic phenomenon, or both. It is only after such patients have been

under treatment and observation for many months that the relation between infection and the existing allergic state becomes clear. A child whose asthma had been controlled by appropriate treatment and who subsequently contracts an upper respiratory infection will stand a better chance of escaping a recurrence of asthma than the child with an uncontrolled case. A mother has frequently insisted that it was not the feather or rabbit hair pillow that was the cause of the asthma, but rather the susceptibility of the child to upper respiratory infection, because during the intervals of freedom from infection the child remained free from asthma in spite of continuous exposure to the sensitizing inhalant substances. This is explained by the fact that these patients have considerable tolerance for the sensitizing proteins under normal conditions. The development of a respiratory infection, however, with its incidental congestion and inflammation of the mucous membranes possibly makes the membrane more permeable to the sensitizing substances.

In this series, a history of recurrent "rhinitis or bronchitis or both" occurring in any season of the year preceded the onset of asthma in twenty-six cases, or 33 per cent, of the allergic group, as follows: In fifteen cases there was a history of "recurrent bronchitis" associated with wheezing, commencing in the fall and winter, and preceding the onset of asthmatic attacks. In seven, asthma was preceded by "recurrent bronchitis" following "a cold in the nose." In the remaining four, asthma followed "upper respiratory infections" in the summer and was not associated with pollen sensitization.

*Sinusitis.*—Simple catarrhal sinusitis probably occurs as frequently as acute rhinitis. Since the clinical symptoms and significance of catarrhal sinusitis are essentially those of acute rhinitis, a discussion of the former condition in its relation to asthma will be unnecessary.

Chronic sinusitis occurs not infrequently as a secondary factor in asthma.

Two patients, or 3 per cent, in the allergic and none in the nonallergic group had chronic suppurative sinusitis. These patients reacted to numerous sensitizing substances, and the part played by the diseased sinuses could not be determined with certainty. Both children also had chronic eczema. The tonsils and adenoids were removed. One of them later developed acute pneumonia. On several occasions asthma was severe and resisted all forms of treatment. For this reason hospitalization was resorted to three times in one case and twice in the other. In each case the asthma cleared within the first forty-eight hours of hospital confinement. The patients continued free from asthma, but the nasal discharge persisted during these periods of hospitalization, which varied from six to eight weeks. Asthma returned the first night they slept at home. It was then clear that the diseased sinuses in these cases were neither a primary nor even a contributory factor in the causation of asthma.

Dean [6] and others reported relief from asthma in children following sinus operation. These reports indicated that the sinus disease was the primary factor in the causation of asthma, notwithstanding the fact that in the majority of these cases no attempt was made to determine the presence or absence of allergy. While it is not within the scope of this paper to discuss the merits of operative intervention in suppurative sinus disease in children with asthma, I am firmly convinced that such intervention should never be undertaken in anticipation of relieving asthma until a thorough investigation of the asthma along the lines of accepted practice has been completed. It is conceivable that a child may be relieved of asthma following appropriate nasal treatment when the sensitizing substances no longer operate as etiologic factors. With this idea in mind, a comprehensive and interesting study was reported by Gottlieb.[7]

*Chronic Bronchitis and Emphysema.*—Sixteen patients of the allergic group had chronic bronchitis and emphysema (volumen pulmonum auctum). In eight of these sixteen patients a deformity of the chest was also present. All the patients of the nonallergic group had varying degrees of chronic bronchitis and four of them had chronic emphysema with resulting deformity of the chest. Thus, the total incidence of chronic emphysema with deformity of the chest was 12 per cent.

It was found that the duration of asthma was not the essential factor in the production of the deformity of the chest. It appeared that the more important factors were the frequency, intensity and the prolonged duration of the attacks.

*Diseased Tonsils and Adenoids.*—For many years the impression has prevailed that enlarged tonsils and hypertrophied adenoids played an important part in the causation of asthma. Holt,[8] Dunn,[9] Koplick,[10] Breitstein [11] and many others favored this contention. Still,[12] among the earlier authors, contended, however, that such an assumption was wholly unwarranted. Still found that of thirteen children on whom tonsillectomy and adenoidectomy were performed in the hope of curing asthma, only one received any benefit from the operation, and in

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6. Dean, L. W.: Paranasal Sinus Disease in Infants and Young Children, J. A. M. A. **85**:317 (Aug. 1) 1925.

7. Gottlieb, M. J.: Relation of Intranasal Disease in the Production of Bronchial Asthma, J. A. M. A. **85**:105 (July 11) 1925.

8. Holt, L. M.: The Diseases of Infancy and Childhood, New York, D. Appleton and Company, 1919.

9. Dunn, C. A.: Pediatrics, Troy, N. Y., The Southworth Company, 1917.

10. Koplick, H.: The Diseases of Infancy and Childhood, Philadelphia, Lea and Febiger, 1918.

11. Breitstein, M. L.: Practice of Medicine, Tice, F., Hagerstown, Md., Prior Co., 1921.

12. Still, C. T.: Common Disorders and Diseases of Childhood, London, Oxford Press, 1912.

this one the good effect was only temporary. In more recent years and especially since the introduction of the protein skin tests, evidence has accumulated pointing to the fallacy of associating tonsils and adenoids with asthma. The latter point of view has been held by Walker,[13] Lintz,[14] Kahn,[15] Rowe,[16] Taylor,[17] Balyeat [18] and others.

In this series, the operation for the removal of tonsils and adenoids was performed on sixty-one children, or 77 per cent, of the protein-sensitive group, and on eleven children, or 52 per cent, of the nonprotein-sensitive group, a total incidence of 72 per cent.

Eighteen patients of the allergic and two of the nonallergic group were operated on prior to the onset of asthma. Since these children presented themselves for the relief of asthma and nasal symptoms, it was evident that the operation failed to accomplish the result intended. On the other hand, in two cases of the allergic and in one of the nonallergic group, a total incidence of 3 per cent, there was a clear history of the onset of asthma immediately following the operation. In the latter case [5] the hypertrophied tonsils and adenoids were part of a general lymphoplasia, and the thymus and tracheobronchial glands were also enlarged.

Forty-three children of the allergic group and nine of the nonallergic group had the tonsils and adenoids removed after the onset of asthma. Of this total, forty-two were operated on before coming under observation, and in none of these cases was the course of the asthma favorably influenced. In one case the nasal symptoms were somewhat lessened. In another the asthma was aggravated. In ten of these cases the tonsils and adenoids were removed after the children came under observation. Well defined indications made the operation necessary. Of these ten patients, seven had been free from asthma for from six months to two years. In none of these was there a recurrence as a result of the operation. Three were operated on during the course of asthma. Two of these children had purulent sinus disease. The nasal discharge in one was lessened, but the asthma was unaffected; in the other the nasal discharge remained the same, and the asthma was aggravated. In the third case there was relief from asthma for two months following the operation, after which it recurred in an aggravated form and has since remained persistent.

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13. Walker, I. C.: A Clinical Study of 400 Patients with Bronchial Asthma, Boston M. & S. J. **179**:288 (Aug. 29) 1918.

14. Lintz, W.: Lack of Operative Indications in Asthma and Other Forms of Allergy, Ann. Surg. **79**:917 (June) 1924.

15. Kahn, I. S., and Grothaus, E. M.: Studies in Pollen Sensitiveness, M. J. & Record **121**:664 (June 3) 1925.

16. Rowe, A. H.: Bronchial Asthma in Children and in Young Adults, Am. J. Dis. Child. **31**:51 (June) 1926.

17. Taylor, W. M.: Bronchial Asthma in Children, South. M. J. **19**:330 (May) 1926.

18. Balyeat, R. M.: Discussion on the paper by Taylor (footnote 17).

*Comment.*—These observations would indicate that enlarged or diseased tonsils and adenoids do not operate as etiologic factors in asthma. On the other hand, surgical intervention may initiate the onset and adversely affect the course of asthma.

Tonsillectomy performed before or after the onset of asthma for the relief of recurrent "head colds" proved to be of no value, because in a great majority of these patients the symptoms were an expression of protein sensitization. Coakley and Pratt [19] and Kaiser [20] concluded that tonsillectomy and adenoidectomy, when definitely indicated, offered a child considerable relief from colds in the head and mouth breathing. This observation is probably true of nonallergic children.

In the case of a child who has asthma and in whom acute recurrent follicular tonsillitis, chronic purulent nasal discharge, mouth breathing or susceptibility to upper respiratory infection coexist, together with enlarged and diseased tonsils and adenoids, an operation is advisable. It is wise, however, to advise the parents that the operation will not relieve the asthmatic condition and may even aggravate it for a time.

### PULMONARY DISEASES

*Acute Pneumonia.*—The rôle that acute pneumonia plays in asthma has received scant attention. In this study an attempt to differentiate whether the pneumonia was lobar or lobular was hopeless for obvious reasons.

The relationship between acute pneumonia and asthma will be discussed under two heads as follows:

1. Pneumonia occurring before the onset of asthma: Two patients of the allergic group had pneumonia before the onset of asthma, with no relationship between the two diseases.

Eight patients of the allergic group and six of the nonallergic group, a total incidence of 14 per cent, gave a definite history of asthma first commencing after or directly associated with an acute pneumonia. The ages of pneumonia, onset of asthma and the age at which each case was first observed are shown in table 1.

Thus, of fourteen cases in which the onset of asthma was associated with pneumonia (table 1), asthma commenced directly after pneumonia in ten, and in the remaining four recurrent bronchitis followed pneumonia and persisted for six months to one year before asthma appeared.

2. Pneumonia occurring after the onset of asthma: Eight children of the allergic group and two of the nonallergic group, a total incidence

19. Coakley, C. G., and Pratt, E. L.: Analysis of the Systemic and Local Conditions Following Tonsillectomy and Adenoidectomy, Laryngoscope **32**:81 (Feb.) 1922.

20. Kaiser, A. D.: Effect of Tonsillectomy on the General Health of Twelve Hundred Children, as Compared with an Equal Number not Operated on, J. A. M. A. **83**:33 (July 5) 1924.

of 10 per cent, contracted pneumonia at varying periods after the onset of asthma. One child of the nonallergic group had pneumonia twice. Three were relieved of their asthma before pneumonia was contracted. They suffered no recurrence as a result of the infection. The others had asthma at the time pneumonia was contracted. It was interesting to note that the asthma in most cases was markedly aggravated during the first days of acute pneumonia, so that a differential diagnosis between the two conditions was difficult to make. The asthma in one case was unaffected, in two it was aggravated, and in the remaining four, with the full development of the pneumonia, the patients became free from asthma and remained free from three to eight months in spite of exposure to etiologic sensitizations.

TABLE 1.—*Fourteen Cases in Which a Definite Clinical Relationship Was Observed Between Acute Pneumonia and the Onset of Asthma**

| | Age | | | |
|---|---|---|---|---|
| Case | Pneumonia | Onset of Asthma | First Observed | Etiologic and Other Current Factors in Asthma |
| **Protein-Sensitive Group** | | | | |
| 1 | 1 | 1 | 10 | Horse dander, chronic bronchitis and emphysema |
| 2 | 1 | 1 | 11 | |
| 3 | 1 | 1 | 5 | Rabbit hair |
| 4 | 1½ | 1½ | 3 | |
| 5 | 2 | 3 | 5 | Rabbit hair |
| 6 | 2 and 3 | 3 | 3 | |
| 7 | 6 | 6 | 12 | Chronic bronchitis and emphysema |
| 8 | 6½ | 7 | 10 | Duck feathers |
| **Nonprotein-Sensitive Group** | | | | |
| 9 | 1½ and 7 | 7 | 12 | |
| 10 | 2 | 2 | 8 | |
| 11 | 2, 3, 6, 8 | 4 | 6 | Chronic bronchitis, emphysema, cylindric bronchiectasis; chronic unresolved pneumonia |
| 12 | 3 | 3 | 5½ | |
| 13 | 5½ | 6 | 12½ | Chronic bronchitis and emphysema |
| 14 | 7 | 7 | 13½ | Chronic bronchitis, emphysema and chronic bilateral unresolved pneumonia |

* Results of roentgenoscopy of the chest in all these patients were negative except in two cases (cases 11 and 14).

*Unresolved Pneumonia.*—Delayed resolution and unresolved pneumonia have been considered by some authors as identical conditions. Delayed resolution, however, does not mean chronicity. Unresolved pneumonia is characterized by its chronic course and resistance to treatment which usually controls delayed resolution. Overend [21] found cases of ill health after pneumonia and infectious diseases among children who were not tuberculous, but whose condition was caused by unresolved pneumonia. Hess [22] concluded that in this type of case tuberculosis was either a primary factor or a complication. With the increasing accumu-

21. Overend, N.: Basal Pneumonic Residues in Children, Tubercle **547**:1 (Sept.) 1920.

22. Hess, J. H.: Unresolved Pneumonias. What Becomes of Them? Arch. Ped. **34**:686 (Sept.) 1917.

lation of publications on this subject in the literature, it is surprising how little attention has been paid to the rôle that unresolved pneumonia plays in asthma. Harkavy,[23] however, stressed this point in the cases of adults and reported nine cases (or 5.6 per cent of a series of 160 cases) of bronchial asthma in which the roentgen-ray shadows were interpreted as being due to unresolved pneumonia. In most of these cases there was a direct relation between the onset of asthma and the antecedent pneumonia. Positive protein skin tests were not obtained in any of these cases.

In this series chronic unresolved pneumonia occurred in two patients of the nonallergic group, a total incidence of 2 per cent. Both of these patients (cases 11 and 14 in table 1) dated their onset of asthma from an antecedent pneumonia. These were undoubtedly true chronic unresolved (nontuberculous) pneumonias, and this condition was the sole etiologic factor in the production of asthma. These patients were relieved of asthma by appropriate treatment. The roentgenograms of these cases will be shown in a future publication.[24]

*Subacute Pulmonary Infiltration.*—In the course of this study it was observed that certain children with asthma presented atypical symptoms which could not be satisfactorily accounted for. Among them was an aggravating cough resistant to usual medication, existing with or independent of the asthmatic state. The physical observations were asthma with bronchitis, and during the intervals of attacks, bronchitis alone. There was no elevation of temperature, and no history of any antecedent febrile illness.

Roentgen-ray shadows of the lungs of these children were interpreted by the roentgen-ray department [25] as "unresolved pneumonia." Since there was no antecedent history of an acute pneumonic process ever having occurred in these children, unresolved pneumonia could not be entertained. This condition I call "subacute pulmonary infiltration," a new term, which, though not accurately descriptive of the condition, is at least not misleading.

Ten cases, or 12 per cent, of the protein-sensitive group and one case, or 5 per cent, of the nonprotein-sensitive group, a total incidence of 11 per cent, showed definite clinical and roentgenographic evidences of subacute pulmonary infiltration.

The age of onset of asthma in relation to the age at which subacute pulmonary infiltration was found, and other important data, are set forth in table 2.

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23. Harkavy, J.: Role of Unresolved Pneumonia in Bronchial Asthma, J. A. M. A. **79:**1970 (Dec. 9) 1922.

24. Peshkin, M. M.: Asthma in Children. V. Roentgenoscopy of the Chest and the Tuberculin Skin Reaction, to be published.

25. Dr. L. Jaches, Director, Roentgen-Ray Department, Mt. Sinai Hospital.

Eight of the eleven cases comprising this group (table 2) were found when the patients were first seen. In five of these eight cases the asthma cleared up after the removal of the sensitizing proteins. In the sixth case (case 3) the base of the left lung was involved, and the presence of

TABLE 2.—*Subacute Pulmonary Infiltration in Children with Asthma*

| Case | Age: Onset Asthma | Age: First Seen | Age: Subacute Pulmonary Infiltration | Symptoms and Observations of Lungs* | Influence on Asthma | Roentgenogram of the Lungs†: Date | Roentgenogram of the Lungs†: Location of Lesion |
|---|---|---|---|---|---|---|---|
| 1 | 1 | 10 | .. | Emphysema with deformity of chest | ..... | 12/16/22 | Negative |
| | | | 12 | Cough, sibilant and sonorous râles | Recurrence | 9/30/24 | Lower part right upper lobe |
| | | | | Persistent cough; few subcrepitant râles and dulness left base; many sibilant and sonorous râles and rhonchi | Recurrence | 11/16/24 | Both bases |
| | | | | ..... | ..... | 2/ 3/25 | Negative |
| 2 | 2 | 3 | 3 | Cough ..... | None | 10/15/23 | Both bases |
| | | | | ..... | ..... | 2/ 7/24 | Negative |
| 3 | 2 | 7 | 7 | Persistent cough, few subcrepitant râles and slight dulness at left base, emphysema with deformity of chest | Unchanged | 4/10/23 | Left base |
| | | | | ..... | ..... | 5/18/23 | Negative |
| 4 | 2 | 11 | .. | ..... | ..... | 7/23/23 | Negative |
| | | | .. | ..... | ..... | 1/17/24 | Negative |
| | | | 11¾ | Persistent cough, subcrepitant râles right base, sibilant and sonorous râles | Recurrence | 5/24/24 | Right base |
| | | | | ..... | ..... | 8/28/24 | Negative |
| 5 | 2½ | 6 | 6 | Cough ..... | None | 10/28/22 | Lower part right upper lobe |
| | | | | ..... | ..... | 11/25/22 | Negative |
| 6 | 3 | 4½ | 4½ | Increased cough ..... | None | 3/17/23 | Right base |
| | | | | ..... | ..... | 11/15/24 | Negative |
| 7 | 4½ | 6½ | .. | ..... | ..... | 6/16/23 | Negative |
| | | | 7 | Persistent cough; few subcrepitant râles left base | Occasional wheeze | 10/13/23 | Both bases |
| | | | | ..... | ..... | 12/14/24 | Negative |
| 8 | 4½ | 14 | 14 | Cough; slight elevation of temperature one day | None | 11/13/23 | Left base |
| | | | | ..... | ..... | 3/10/24 | Negative |
| 9 | 7½ | 9 | 9 | Increased cough; sibilant and sonorous râles and rhonchi | Aggravated | 8/16/22 | Right base |
| | | | 9¾ | Same as above..... | Aggravated | 5/31/23 | Left base |
| | | | 10¾ | Spasmodic cough ..... | None | 5/ 8/24 | Right base |
| | | | 11 | Cough; sibilant and sonorous râles | Recurrence | 8/11/24 | Negative |
| 10‡ | 8 | 10 | 10 | Increased cough; slight dulness both bases; sibilant and sonorous râles; emphysema with deformity of chest | Aggravated | 4/13/23 | Both bases |
| | | | | Sibilant and sonorous râles ..... | ..... | 10/29/23 | Negative |
| 11 | 9 | 10 | 10 | Persistent cough ..... | None | 11/13/23 | Right base |
| | | | | ..... | ..... | 3/10/24 | Negative |

* Only positive symptoms and observations of the lungs are recorded.
† The roentgenograms will be shown in a future publication.[24]
‡ Nonprotein-sensitive case; the remaining cases are protein-sensitive.

the infiltration had no effect on the course of the asthma. Under appropriate treatment, the asthma cleared up. One year later there was an involvement of the base of the right lung, and the asthma recurred. In the seventh patient (case 9) involvement of the base of the right lung

caused a decided aggravation of the asthma. After appropriate treatment for desensitization, the asthma was markedly relieved. Nine months later, the asthmatic condition was again aggravated, and at this time the base of the left lung was found to be involved. The child improved again, and one year later, when the patient was entirely free from asthma, a spasmodic cough set in, but it was quickly controlled. Roentgenoscopy of the chest showed again an infiltration of the base of the right lung. Several months later the child began to suffer with asthma again, but the roentgenograms were negative. The eighth case (case 10) was that of the only nonprotein-sensitive patient of this group, who was brought to the clinic because of the increase in the severity of his asthma. In this patient the bases of both lungs were found to be involved.

In three patients subacute pulmonary infiltration was found from six months to two years after they were first observed. When the patients were first observed, routine roentgenograms of the chest did not show any abnormality. In two of these cases, the infiltration caused recurrence of asthmatic attacks; in the third, there was only coughing and slight wheezing.

None of these patients showed any clinical evidences of acute pneumonia. The great majority of them were not even subacutely ill. In only two (cases 9 and 10), there was a slight elevation of temperature which lasted from one to two days.

The cough lasted several weeks and did not yield to the usual medication. This type of cough was the one constant symptom found. The physical observations in the lungs were not definite enough to form a basis for diagnosis. It is interesting to note that this condition occurred fifteen times in the eleven cases, as follows: in the right base, 6; in the left base, 3; in both bases, 4; and in the lower part of the right upper lobe, 2. About one half of these patients did not suffer a recurrence of asthma. Without any particular medication the infiltration required from four to eight weeks to clear. None of these infiltrations were tuberculous in nature.

On the basis of the foregoing observations, I feel justified, at least for the present, in differentiating subacute pulmonary infiltration from that caused by unresolved pneumonia, resolving pneumonia or delayed resolution.

*Other Contributory Factors.*—Physical overexertion is probably one of the most important nonspecific factors in asthma of childhood. A child who has been relieved of asthma may suffer a recurrence following exertion, such as climbing stairs hurriedly, running or jumping.

Indiscretion in diet, such as overeating, eating hurriedly and at irregular intervals or the eating of improperly prepared food, are factors that play some rôle in asthma. The ingestion of such foods as sweet corn,

cheese (excepting cream cheese), goose, turkey, pork, radish, mustard, cucumber, pickle, bean, cooked cabbage, mushroom, parsnip, squash, turnip, sweet potato, herring, salmon, sardine, bluefish, tunafish, berries of all kinds, grape, cherry, melons and delicatessen food, are frequently responsible for inducing or aggravating an attack of asthma. Perhaps one of the most frequent contributory causes of asthma is the drinking of cold liquids and the eating of ice cream. When the body is overheated following exertion, the drinking of iced liquids is dangerous. This practice is naturally most common during the summer months.

The variation of weather conditions and the changes of season are nonspecific factors of asthma, probably because of the increased tendency to upper respiratory infections at these times. Exposure to wind, especially on a cold day, often induces attacks of asthma.

Exposure to a freshly painted room invariably invites trouble. Emotional upsets are not an important factor in childhood.

*Comment.*—Extensive experience in treating allergic diseases forces the realization that protein sensitization alone does not entirely explain the varied manifestations associated with allergy. It has been demonstrated that 10 per cent of the children with asthma [1] who were skin sensitive to various proteins showed no etiologic connection between protein sensitization and the asthma. Again, in those patients in whom protein sensitizations were found to be of etiologic importance, it was evident that these sensitizing substances were only exciting factors and not the basic cause of symptoms. Many authors regard the basis of allergy as a disturbed balance between the sympathetic and parasympathetic nervous systems. A more logical conception of allergy would be that there exists within the body a physiochemic disturbance which probably manifests itself through the nervous system. If the body is in a state of physiochemic equilibrium the allergic patient enjoys freedom from symptoms in spite of exposure to an etiologic protein. Such a patient is said to have acquired a protein tolerance. Failure to appreciate that fluctuating variations of tolerance exist in different patients as well as in the same patient leads to misinterpretation of the rôle that protein sensitization plays in asthma. Vaughan [26] looks on these subjects during the intervals of freedom from symptoms as being in a "balanced allergic state." "Balanced physiochemic state" is (at least for the present) a better term, because it can include all forms of asthma.

If any factor is allowed to overthrow this governing mechanism, symptoms will result. These factors may be specific or nonspecific, or both. The specific factor may be an overdose of the sensitizing protein. A child was continually exposed to rabbit hair, which was of major

26. Vaughan, W. T.: Interaction of Specific and Nonspecific Factors in Allergic Disease, Virginia M. Monthly **51**:472 (Nov.) 1924.

importance in the causation of attacks of asthma, which occurred at bimonthly intervals. One day he visited a neighbor at a time when he was free from all symptoms. He playfully and vigorously bounced on the seat of a Morris chair. Within several minutes he began to sneeze and soon was seized with violent asthma which resisted all treatment, including hospitalization for several days. Investigation revealed that the seat of the chair was stuffed with rabbit hair.

Other illustrations of overdosage can be found in children who ingest too much of one or moderate amounts of several sensitizing foods at the same meal. It has been observed that rabbit hair in sensitized patients may induce asthma almost immediately after exposure. Again, the symptoms may not develop until a period varying from six months to four years has elapsed, in spite of constant exposure. This can be explained only by the fact that in the first instance the physiochemic equilibrium was completely unbalanced, and in the latter instances it took from six months to four years of constant irritation to induce physiochemic unbalance, resulting in definite symptoms.

The protective mechanism which maintains the physiochemic balance may also become disturbed through nonspecific causes. It has already been stated that various conditions and diseases are often the determining factors in initiating the onset of asthma. If exposure to the sensitizing protein is insufficient to disturb the physiochemic equilibrium, an intercurrent infection is often sufficient to produce complete unbalance. However, in the absence of exposure to the sensitizing substance, an intercurrent infection will not produce asthma in the presence of a partially restored balance.

When the physiochemic unbalance was profoundly disturbed, the various nonspecific factors always induced asthma, in spite of the fact that the patient was receiving appropriate specific treatment at the time. In these cases there is little that can be done in giving relief until Nature itself restores the physiochemic balance. A boy in whom horse dander was the major etiologic sensitization, and in whom the asthma could not be controlled by specific or any form of nonspecific treatment, was finally sent to the country. After the first week his asthma cleared. Later he found that riding horses did not cause a recurrence of asthma. At the end of four months, he returned to his former environment in the city, where he has continued to remain free from asthma, now more than two years.

Many seeming paradoxes occur in the treatment of asthma. Definitely specific cases frequently do not respond to specific therapy. Again, an uncontrollable case may clear up without any treatment or by some treatment regarded as purely nonspecific. In order to evaluate intelligently the failures as well as the successes, one must have a logical conception of the various specific and nonspecific factors in asthma,

etiologic and contributory; and, most important of all, one must realize that in the final analysis relief from asthma can be accomplished only by restoring the patient's physiochemic balance.

## CONCLUSIONS

1. Among the diseases and conditions responsible for initiating the onset of asthma were the following: pertussis, 15 per cent; acute pneumonia, 14 per cent; measles, 4 per cent; tonsillectomy and adenoidectomy, 3 per cent; and scarlet fever, 2 per cent—a total incidence of 38 per cent.

2. Measles, acute pneumonia and diphtheria had a temporarily beneficial effect on the course of asthma. Pertussis aggravated asthma.

3. The incidence of chronic bronchitis and emphysema with deformity of the chest was 12 per cent, and without deformity of the chest it was 8 per cent, a total incidence of 20 per cent. The frequency, intensity and the prolonged duration of attacks were the factors principally responsible for the production of deformity of the chest rather than the duration of the asthmatic state.

4. Hypertrophied and diseased adenoids and tonsils did not operate as a causative factor of asthma. In 3 per cent of the cases tonsillectomy and adenoidectomy aggravated the asthma. The removal of tonsils and adenoids did not relieve asthma except in one instance, and in that the relief was only temporary.

5. Chronic unresolved pneumonia as an etiologic factor occurred in 2 per cent of the cases in the entire series. These patients definitely dated their asthma from an antecedent pneumonia. They were protein nonsensitive and were not tuberculous.

6. Subacute pulmonary infiltration (a new term) occurred in 11 per cent of the cases. A summary of the observations is as follows: There was an aggravating cough of several weeks' duration, resisting usual medication and existing with or independent of the asthmatic state. The physical signs were asthma with bronchitis and, between attacks, bronchitis alone. There was, as a rule, no elevation of temperature. Roentgenoscopy of the lungs showed shadows which cleared within two months without any particular treatment. These shadows did not appear to be different from those seen in delayed resolution, resolving or unresolved pneumonia. In all of these patients there was a negative history of an antecedent pneumonia, and all were nontuberculous.

7. Physical overexertion, indiscretion in diet, especially the eating of ice cream and the drinking of iced liquids, variations of weather, the change of seasons and exposure to winds and freshly painted rooms were important contributory factors in inducing asthmatic attacks.

8. Allergy per se cannot be explained entirely on a basis of protein sensitization, because the sensitizing substances in themselves are merely exciting factors and not the basic cause of symptoms. A patient in a state of "physiochemic equilibrium" enjoys freedom from symptoms in spite of exposure to etiologic substances. If any factor overthrows this governing mechanism, symptoms will appear. These factors may be specific or nonspecific, or both. The appreciation of this fact will aid toward establishing a clearer conception of asthma and lay the foundation for a more intelligent management of the disease in childhood.

9. The association of pertussis, measles, scarlet fever, acute pneumonia and tonsillectomy and adenoidectomy with the onset of asthma in the cases of this series is sufficiently striking to command attention from the standpoint of prophylaxis. If a child contracts any of these diseases or undergoes an operation for the removal of tonsils and adenoids, and there is an allergic family history, especially with an antecedent eczema, angioneurotic edema or "recurrent rhinitis and bronchitis," the elimination of the known sensitizing substances from the environment and diet may prevent the onset of asthma.

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# BACTEREMIA IN DIPHTHERIA

## INVASION OF THE BLOOD STREAM BY THE KLEBS-LOEFFLER BACILLUS AND ASSOCIATED ORGANISMS *

EDGAR MARTMER, M.D.
DETROIT

The work of the earlier investigators was so brilliant that further investigation of the disease process that is known as diphtheria has often been regarded as a subject concerning which further investigation would be unprofitable. Diphtheria, however, is a disease that still presents many unsolved problems in medicine and public health.

Many of the statements regarding this disease which appear in the various textbooks have been copied from previous editions and earlier authors to such an extent that their value is questionable. One statement in particular has been handed down through the years and that is that *Bacillus diphtheriae* is always localized at the site of the lesion and does not invade the blood stream. It is unquestionably true that early in the disease the organism is localized, and if at this time specific treatment in the form of antitoxin is instituted, or if the case is a mild one occurring in a patient with good powers of resistance, it progresses no further.

When, however, treatment is begun late in the infection, at a time when the patient's resistance is low, in cases of marked severity, and particularly in the cases in which the organisms tend to multiply rapidly rather than to produce a toxin of marked potency, and finally in those in which secondary infection or invasion by the streptococcus, staphylococcus or pneumococcus aids in the dissemination of the organisms, there is a greater probability of encountering a systemic infection. In such cases, the presence of a greater or less number of bacteria in the blood stream is to be expected. This fact has long been recognized by certain investigators but has not been brought to the attention of the medical profession as a whole.

Among the workers in this field reporting large series of blood cultures, the foremost are Leede [1] and Roedelius.[2] Taking their observations as a group it was found that the Klebs-Loeffler bacillus was found three times in 313 cases during life. The majority of this series were mild cases. In the cases from which positive cultures were obtained,

* Received for publication, Jan. 17, 1927.

1. Leede, W.: Bakterologische Blubefünde bei Diphtherie, Ztschr. f. Hyg. u. Infektionskrankh **62**:225 1911; Beiträge zur Diphtherie mit besonderer Berücksichtigung der pathologisch-anatomischen Organe und bakteriologischen Leichenblutbefünde in ihrem Verhalten zum klinischen Bilde, Ztschr. f. klin. Med. **77**:297, 1913.

2. Roedelius, E.: Ueber das Vorkommen von Diphtheriebazillen im stomenden Blut, Ztschr. f. Hyg. u. Infektionskrankh. **75**:497, 1913.

all were of the severe type. Both of Roedelius' cases were of the hemorrhagic type. In these two cases, no operative procedure had been done, and the bacilli were in pure culture, while in Leede's case they were mixed with streptococci.

Neissen,[3] having recovered *Bacillus diphtheriae* in pure culture from the blood of a boy, aged 9 years, published the first report of a case of antemortem blood stream infection. The organism was not subjected to tests for pathogenicity.

Roosen Runge [4] reported a case that was probably a true septicemia since the first culture was confirmed by a second positive culture and the finding at postmortem of an ulcerative endocarditis in which *Bacillus diphtheriae* was demonstrated.

Mahler [5] secured the organism in two out of three cultures in his case, indicating either a considerable scarcity of the organisms or an inconstancy of the invasion.

Ucke's [6] report was based on the discovery of a single colony morphologically of *Bacillus diphtheriae* in one of several tubes of media inoculated with the patient's blood by a confrère and brought to him for examination. A second culture was negative.

Hesse [7] obtained a positive blood culture in a patient who developed an ulcerative endocarditis demonstrated to be due to *Bacillus diphtheriae*.

Morgan [8] records a case in which he isolated an organism corresponding to *Bacillus diphtheriae* from the venous blood thirty-six hours antemortem.

H. Windsor Wade [9] reports a case of an obscure fever thought at first to be bubonic plague in which the blood culture taken twenty-two hours before death yielded a virulent growth of diphtheria bacilli.

It is extremely interesting to note that in the cases reported as instances of antemortem invasion of the blood stream by *Bacillus diphtheriae*, the organisms were either nonvirulent or of extremely low virulence in the four cases in which animal tests were made. These cases were those of Roosen Runge, Mahler, Ucke and Morgan.

The evidence obtained by bacteriologic examination at autopsy is conflicting. For example, while Frosch [10] found the blood positive in

3. Neissen: Wien. med. Wchnschr. **47**:2221, 1902.

4. Roosen Runge: Ein Fall von Diphtherie-Bazillensepsis, München. med. Wchnschr. **50**:1252, 1903.

5. Mahler, P.: Ueber einen Fall von Diphtherie-Bazillen und Streptokokken Sepsis, Berl. klin. Wchnschr. **44**:1499, 1907.

6. Ucke: Centralbl. f. Bakteriol. **46**:1499, 1908.

7. Hesse, F.: Diphtherie-Bazillen als Sepsiserreger, Deutsche med. Wchnschr. **35**:1096, 1909.

8. Morgan, E.: Diphtheria Septicemia with Report of a Case, Am. J. Dis Child. **5**:317 (April) 1913.

9. Wade, H. W.: Bacteriemia Due to the Bacillus Diphtheriae, J. Infect. Dis. **16**:292, 1915.

10. Frosch, P.: Die Verbreitung über Infection durch kutane Impfung bei Tieren, Arb. a. d. k. Gsndhtsamte. **18**:453, 1893.

thirteen cases out of fourteen, Reiche [11] found only twenty-six positive out of 586 cases.

Some authors have suggested that insufficient attention often was paid to the danger of contamination of the various organs by mere handling during demonstrations, etc., and it will be recalled that Loeffler,[12] who recovered *Bacillus diphtheriae* from a human liver, ascribed this result to a contamination by the trachea which had been placed on it during the autopsy.

Liedtke and Volckel [13] attribute their success to special forms of technic and found that all the organs contained the bacilli. They ground up large fragments of the organs and separated the bacilli by the petrol ether method described by H. Conradi.[14]

Pearce [15] made cultures from the heart's blood, spleen, liver and kidneys of a large number of fatal cases of diphtheria and diphtheria complicated by scarlet fever, measles, and broncho-pneumonia and found the diphtheria bacillis in one or more sites in a fairly large number of cases, either alone or in conjunction with streptococci. The latter organism was found alone in a larger number of cases than was *Bacillus diphtheriae,* particularly in those cases complicated by scarlet fever and measles. He reports a total of 140 cases, in six of which the diphtheria bacillus was found in the heart's blood. In three cases it was in pure culture and in the remaining cases it was mixed with streptococci.

Howard [16] describes carefully an interesting case of ulcerative endocarditis due to the diphtheria bacillus in which the point of entry was not determined. Cultures made from the various organs and sections of the tissues removed eight hours postmortem showed the bacillus.

Owing to the difference in technic and the omissions in descriptions of the various authors, it is impossible to make any general comparisons between their results or even to estimate their value accurately.

The fact emerges, however, that *Bacillus diphtheriae* has been found in the blood and in all the organs. As an indication of the frequency of positive results, it may be mentioned that in the largest series of cases, 586 reported by Reiche in 1914, about 4 per cent were positive for the

11. Reiche, F.: Die Hamburger Diphtherie epidemie 1909-1914, Ztschr. f. klin. Med. **81**:199, 1914.

12. Loeffler, F.: Untersuchungen über unincedentungsher Mikroorganismen für die Entstehung der Diphtherie beim Menschen, beim Taube und beim Kalbe, Mitth. a. d. k. Ganhtsamte **2**:421, 1884.

13. Liedtke and Volckel: Ueber Befunde von Diphtherie Bazillen in den Organen tödtlich verlaufener Diphtherie, Deutsche med. Wchnschr. **40**:594, 1914.

14. Conradi, H.: Ueber ein neues Prinzip der electiven Zuchtung und seine Anwendung bei Diphtherie, München. med. Wchnschr. **60**:1073, 1913.

15. Pearce: J. Boston Soc. M. Sc. **2**:92, 1898.

16. Howard: Am. J. M. Sc. **108**:651, 1894.

organism; a similar percentage was found by Bonhoff [17] in 322 cases. In the fourteen cases reported by Frosch,[12] the five cases of Federici [18] and the seven cases of Leidtke and Volckel,[15] practically 100 per cent were positive for the organism. The bacilli are described as being scarce and requiring large quantities of inoculum for their demonstration. In the large series of Reiche, the bacilli were mixed in the blood with other organisms in nine cases and were obtained in pure culture in seventeen. In Bonhoff's series, only three of the cultures were pure and the remaining seventeen were mixed with streptococci.

In addition to those already mentioned, the following authors have described diphtheria bacilli in the blood: Kolisko and Paltauf,[19] Booker,[20] Canon,[21] J. H. Wright,[22] Wright and Stokes,[23] Stokes,[24] Nowak,[25] Kanthack and Stephens,[26] Barbier and Tollemer,[27] Glucksmann,[28] Richardiere, Tollemer and Ullman,[29] Braun and Thiry,[30] Plange and Schmitz,[31] and Rottger.[32]

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17. Bonhoff, F.: Ueber das Vorkommen von Virulenten Diphtherie Bazillen im Blut und in der Cerebrospinal Flüssigkeit des Menschen, Ztschr. f. Hyg. u. Infektionkrankh. **67**:349, 1910.

18. Federici, F.: Sulla presenza del bacillo del Loeffler mel sangue dei difterici, Arch. ital. di clin. med. **33**:11, 1894.

19. Kolisko, A., and Paltauf, R.: Zum Wesen der Croups und der Diphtherie, Wein. klin. Wchnschr. **2**:147, 1889.

20. Booker, W. D.: As to the Aetiology of Primary Pseudo Membranous Inflammation of the Larynx and Trachea with Remarks on the Distribution of Diphtheria Bacilli in the Organs of the Body Distant from the Seat of Local Infection, Arch. Pediat. **10**:642, 1893.

21. Canon: Bacteriologische Blutuntersuchungen bei Sepsis, Deutsche med. Wchnschr. **19**:1038, 1893.

22. Wright, J. H.: Studies in the Pathology of Diphtheria, Boston M. & S. J. **131**:329, 1894.

23. Wright, J. H., and Stokes, W. R.: A Report of the Bacteriological Examination of Autopsies, Boston M. & S. J. **32**:271, 293-330, 1895.

24. Stokes, W. R.: The Bacteriological Examination of Nine Autopsies on Cases of Diphtheria Treated with Antitoxin, Boston M. & S. J. **133**:581, 1895.

25. Nowak, J.: Blutfunde bei an Diphtherie verstorbenen Kindern, Centralbl. f. Bakteriol. **19**:982, 1896.

26. Kanthack, A. A., and Stephens, J. W. W.: The Escape of Diphtheria Bacilli into the Blood and Tissues, Tr. Path. Soc. **47**:361, 1896; J. Path. & Bacteriol. **7**:4, 1896.

27. Barbier, H., and Tollemer: Nouvelles recherches bacteriologiques chez les diphtheriques; infection bacillaire, reinfection septiques, Bull. et mém. Soc. méd. d. hôp. de Paris **14**:1218, 1897.

28. Glucksmann, S. J.: Ueber die bakteriologische Diagnose der Diphtherie, Ztsch. f. Hyg. u. Infektionskrankh. **26**:417, 1897.

29. Richardiere, Tollemer and Ullman: Nouveaux faits de présence du bacille diphtherique dans le sang et dans les centres nerveux bulbo-protuberantiels, Bull. et mém. Soc. méd. d. hôp. de Paris **15**:22, 1898.

30. Braun, H., and Thiry, G.: Septicemie diphtherique, Gaz. d. hôp. **72**:476, 1899.

31. Plange, W., and Schmitz, H.: Ueber das Vorkommen und die Verbreitung von Diphtheriebazillen im menschlichen Körper, München. med. Wchnschr. **62**: 395, 1915.

32. Rottger, W.: Ueber Befünde von Diphtheriebazillen in der menschlichen Milz bei tödtlich verlaufener Diphtherie, Centralbl. f. Bakteriol. **1**:161, 1918.

Thus it will be seen that *Bacillus diphtheriae* has been isolated from the blood by a large number of workers; however, the work of many is open to the criticism that they have not proved the virulence of their organism by animal inoculation.

## EXPERIMENTS

In an attempt to repeat the work of these earlier investigators, I made a series of blood cultures on patients with diphtheria who were admitted to the Herman Kiefer Hospital during the winter of 1925-1926.

The patients selected were those who had not had any antitoxin previous to admission and who were not selected with regard to the severity of the condition or the length of time they had been sick. Blood cultures were taken immediately on admission and before antitoxin was administered.

The blood was withdrawn from the veins of the elbow except in the case of small children in whom it was found much easier to take it from the jugular veins. At least 10 cc. was withdrawn and immediately placed in the culture mediums. The flasks were incubated for at least twelve hours before examination and if sterile were reincubated and examined at the end of twenty-four, forty-eight and seventy-two hours. It was thought best to use a liquid medium, so a 1 per cent glucose broth was used. In those cultures presenting growth, subcultures were made on Loefler's blood serum and blood agar plates.

Cultures were made in a series of forty cases, and of these six showed a blood stream infection. Three presented pure cultures of *Bacillus diphtheriae* and the others a hemolytic streptococcus. These cultures were all found positive at the end of the first twenty-four hour period of incubation.

It is interesting to note that two of the cases presenting infection with *Bacillus diphtheriae* were true hemorrhagic diphtheria, and the third case showed hemorrhages from the nose and oral mucous membranes before death. None of the patients who showed infection with the streptococcus had hemorrhages, and they were all of the so-called septic type of diphtheria.

## CONCLUSIONS

From a résumé of the literature and the work that I have done, I feel that the following conclusions are not unjustified:

1. Diphtheria is at times complicated by a blood stream infection.
2. *Bacillus diphtheriae* may invade the blood stream in severe cases.
3. The septic type of diphtheria may be caused by a streptococcic septicemia complicating diphtheria.
4. Hemorrhagic diphtheria probably is caused by a *Bacillus diphtheriae* bacteremia.

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# ESSENTIAL THROMBOCYTOPENIA

## REPORT OF A CASE IN AN INFANT AGED FOUR MONTHS *

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Essential thrombocytopenia or morbus maculosus werlhoffii has its onset, as a rule, during the school age period. Finkelstein [1] states that the disease usually has its onset at from 6 to 10 years of age, and that its occurrence in infancy is extremely rare; indeed, he makes no mention of the disease in his textbook.[2] Griffith [3] writes that the disease is uncommon in infancy and is most often seen in children after the age of 3. Lucas [4] mentions no age limit. Hirschfeld [5] states that the disease has its onset in the school age period and often somewhat later. Schilling [6] makes no mention of the age at which the disease may begin.

Giffen and Halloway [7] review twenty-eight cases in which splenectomy had been performed, the youngest patient being 2½ years of age. Landsberger [8] reports a case of purpura with hemorrhages into the skin and mucous membranes due to an idiosyncrasy to cow's milk in an infant 6 months old. A reduction in the number of platelets, prolonged bleeding time, and failure of retraction of the clot were present for only a short time, however, and the author does not regard it as a true case of morbus maculosus werlhoffii but includes it in the group of anaphylactoid purpuras; in fact, Glantzman [9] frequently observed a temporary reduction of blood platelets in his cases of anaphylactoid purpuras.

Waltner [10] reports a case of congenital morbus maculosus werlhoffii in a new-born infant whose mother presented evidences of the disease in the later months of pregnancy. In his review of the literature, he states that the youngest patients thus far reported were those of H. Nocke [11] and Glantzman.[12] Nocke's case occurred in an infant, aged 14 months, who manifested symptoms of the disease ten days

* Received for publication, Feb. 3, 1927.

* From the Pediatric Service of the United Israel Zion Hospital.

1. Finkelstein: Jahreskurse für ärtzliche Fortbildung, June, 1921.
2. Finkelstein: Text Book of Diseases of Infants, ed. 3, Berlin, Julius Springer, 1924.
3. Griffith: The Diseases of Infants and Children, vol. 2, p. 478.
4. Lucas in Abt's Pediatrics, 1924, vol. 4, p. 539.
5. Hirschfeld: Lehrbuch der Blutkrankheiten, Berlin, A. Hirschwald, 1918.
6. Schilling: Das Blutbild und seine klinische Verwertung, Jena, Fischer, 1926.
7. Giffen and Halloway: Am. J. M. Sc. **170**:186, 1925.
8. Landsberger: Ztschr. f. Kinderh. **39**:569, 1925.
9. Glantzman: Jahrb. f. Kinderh. **84**:308, 1916.
10. Waltner: Jahrb. f. Kinderh. **106**:307, 1924.
11. Nocke, H.: Monatschr. f. Kinderh. **19**:455 (March) 1921.
12. Glantzman: Jahrb. f. Kinderh., 1914, vol. 83; 1918, vol. 88.

after vaccination; Glantzman's patient was 15 months old. Waltner also makes brief mention of a case in an infant aged 1 year, who was under treatment at the clinic at that time. The following case is reported because a search of the literature reveals the fact that it represents perhaps the youngest infant with acquired essential thrombocytopenia.

## REPORT OF CASE

HISTORY.—M. L., a white female infant, aged 4½ months, born in this country, of Jewish parents, was brought to my office for examination on June 1, 1926. The chief complaint was repeated expistaxis. The family history was negative; i. e., the father and mother at no time evidenced tendencies to hemorrhage.

The infant was born at term after a normal delivery; the weight at birth was 6 pounds (2,727.5 Gm.). The infant was breast-fed exclusively until May 8, 1926, when complementary feedings were added; these consisted of six feedings of 2 ounces each of a mixture of cow's milk and one-third water, with the addition of 5 per cent dextrimaltose. The infant made normal gains in weight during this period. During the early part of April, prior to the change in feeding, the mother noticed that the infant had a nose bleed and that epistaxis occurred about once a week thereafter. Blood in the stools was also observed once. The amount of blood lost could not be determined. The mother also stated that areas of ecchymosis frequently appeared on the child's body without any apparent injury or pressure.

*Physical Examination.*—The infant's general condition was good; the weight was 13 pounds and 14 ounces (6,293.6 Gm.). Pallor was not present; turgor and muscle tone were good, and the infant was quite active. Petechiae were present on the forehead and on the lower extremities from the hips to the toes. There were large ecchymotic areas over the buttocks, arms and back. The nasal mucous membrane was examined; ulceration was not found. The cervical, axillary and inguinal glands were not enlarged. The spleen was felt 2 cm. below the free border of the ribs; the liver was palpable 3 cm. below the costal border. Craniotabes and beading were not present. The reflexes, the heart and lungs were normal. The capillary resistance test was strongly positive. Hospitalization for the purpose of further study was recommended, and the infant was admitted to the hospital on June 2, 1926. Examination of the blood revealed: red blood cells, 2,500,000, moderate poikilocytosis; hemoglobin, 40 per cent; color index, 0.8; white blood cells, 29,000, 80 per cent being lymphocytes and 20 per cent polymorphonuclear leukocytes; platelets, 20,000; coagulation time, four minutes; bleeding time, twelve minutes; retraction of clot, absent after eight hours. The Wassermann test was negative. The urine was normal. A diagnosis of purpura hemorrhagica of the thrombocytopenic type was made, and 40 cc. of whole blood from the father was injected intragluteally. As the infant was breast-fed and as accommodations for the mother's stay could not be made, the patient was discharged from the hospital on June 4.

*Subsequent Course.*—On June 6, the infant had moderate epistaxis, and new purpuric spots appeared on both arms. On June 7, petechiae were present on both buttocks. On this day, 20 cc. of whole blood was again injected intramuscularly. On June 11, epistaxis occurred again but no intestinal bleeding was noticed. On June 12, the child accidentally received a slight blow on the nose, and a large ecchymotic area developed over the nose and forehead. On June 14, no petechia or other evidences of hemorrhage were visible, except for the ecchymotic area on the nose and forehead previously mentioned. Twenty cubic centimeters of whole blood was injected intramuscularly at this time.

On June 21, the infant was again brought for treatment, and the mother reported that epistaxis and slight bleeding from the rectum had occurred two days previously. Physical examination, however, did not reveal any evidence of

bleeding into the mucous membranes or the skin. Fifteen cubic centimeters of whole blood was injected intramuscularly at this time. On July 12, the infant was seen again; the mother stated the baby had had an elevation of temperature which lasted three days, from July 3 to July 6, and which ranged from 102 to 104 F.; that unusual symptoms were not present during this period, and that bleeding had not occurred since June 21. Examination at this time (July 12) revealed that the infant was in splendid condition, weighing 15 pounds and 2 ounces (6,860.5 Gm.)—a gain of 1 pound and 4 ounces (567 Gm.) in about six weeks. The capillary resistance test, however, was still strongly positive, and it was therefore thought advisable again to inject 35 cc. of whole blood intramuscularly.

On July 20, a second examination of the blood revealed: red blood cells, 4,250,000; white blood cells, 8,200, 79 per cent being lymphocytes and 21 per cent polymorphonuclear leukocytes; hemoglobin, 60 per cent; color index, 0.71; bleeding time, eight minutes; coagulation time, six minutes; retraction of the clot, absent after six hours; platelets, 140,000.

Thus it may be observed that with the rise in the number of platelets, bleeding had ceased. The infant has remained well up to the present writing.

Examination of the blood on November 25 revealed: red blood cells, 5,280,000; white blood cells, 15,200; hemoglobin, 74 per cent; color index, 0.7; bleeding time, four minutes; coagulation time, six minutes; platelets, 160,000; retraction of clot—present after one hour.

## COMMENT

Infants or young children suffering from purpura hemorrhagica, while manifesting hemorrhages elsewhere in the body, are particularly prone to nasal hemorrhage. The hemorrhages may be spontaneous or they may occur following the slightest trauma. Temporary elevations of temperature frequently occur without apparent cause, as in the case reported. The general condition of the children, in spite of the bleeding, usually remains good; in fact, this infant made normal, regular gains. The spleen is moderately enlarged in some cases; in others it is not. The course of the disease is characterized by exacerbations and remissions, and bleeding may stop spontaneously without any treatment. One must be guarded, therefore, in attributing curative properties to one particular method of treatment until the infant has been observed for a sufficiently long time. During an exacerbation, the platelets always drop to 30,000 or below, and begin to increase when the remission sets in. As is well known, the three characteristic features of the blood picture are:

1. A reduction in the number of blood platelets and a change in their appearance (degenerative forms).

2. The increased bleeding time.

3. The failure of retraction of the clot or prolonged retraction time of the clot.

In young infants, the disease must be differentiated from hemorrhagic disease of the new-born. Von Reuss [13] states that hemorrhagic

13. Von Reuss: Die Krankheiten des Neugeborenen, Berlin, Julius Springer, 1914, p. 396.

disease of the new-born is characterized by the fact that it always occurs during the first ten days of life, that bleeding is severe, as a rule leading rapidly to a severe anemia, and that the hemorrhages most often occur in the gastro-intestinal tract. The blood picture, too, is different in hemorrhagic diseases of the new-born; while there may be an increased bleeding time in both conditions, there is no reduction in the number of platelets; nor is there a failure of retraction of the clot in hemorrhagic diseases of the new-born. In the case reported, evidence of bleeding did not occur until the infant was 2 months old. The disease may be confused with lymphatic leukemia, particularly if the blood is examined after a severe hemorrhage, when a sharp rise in the number of white cells is likely to occur, with a preponderance of lymphocytes (as shown in the first examination of the blood). Essential thrombocytopenia must also be differentiated from hemophilia. Minot [14] states positively that true hemophilia never occurs in females; nor does it occur at such an early age. In addition, the coagulation time is definitely prolonged in hemophilia, while in purpura hemorrhagica it is normal. Failure of retraction of the clot or increased retraction time and a reduction in the blood platelets do not occur in hemophilia.

Many theories have been advanced as to the pathogenesis of this disease. Minot [14] considers the disease "to be a chronic insufficiency of the blood platelets, or a congenital hypoplasia of the marrow or insufficiency of the marrow with special involvement of the platelets." Frank [15] and Glantzman [16] regard it as due to a primary myelopathy. Kaznelson [17] regards the disease as due to a hyperfunction of the blood platelet destroying function of the spleen and therefore advocates extirpation of this organ as the best method of treatment. Subsequently, Brill and Rosenthal [18] recommended splenectomy as the best method of treatment; it should be emphasized, however, that while an increase in the number of platelets occurs immediately following splenectomy, this increase is only temporary and the count falls rapidly at a later period. The effect on the cessation of hemorrhages, however, is excellent in spite of the decreased number of platelets. Brill and Rosenthal have observed that the cessation of bleeding is at times miraculous, occurring immediately after the splenic vessels are ligated and while the patient is still on the operating table.

Finkelstein,[1] however, is of the opinion that extirpation of the spleen should be left for the severe, chronic cases that have failed to respond to repeated transfusions or to roentgen-ray irradiations of the spleen

14. Minot, quoted by Lucas: Abt's Pediatrics, 1924, vol. 4, p. 540.
15. Frank: Berl. klin. Wchnschr. **21**:556, 1916.
16. Glantzman: Jahrb. f. Kinderh. **83**:390, 408, 1916.
17. Kaznelson: Ztschr. f. klin. Med. **87**:133, 143, 1919.
18. Brill and Rosenthal: Am. J. M. Sc. **166**:503, 1923.

with stimulating doses. He states that while a temporary rise in the number of platelets occurs and a marked diminution in the tendency to bleeding takes place after splenectomy, the improvement is not permanent, because accessory spleens and the extrasplenic reticulo-endothelial system (retroperitoneal glands, Kupffer's stellate cells) assume the function of the extirpated organ.

Although Brill and Rosenthal [18] state that the transfusion and the injection of whole blood are of no value and may even be harmful by increasing hemorrhage, it seems that this infant was benefited, at least temporarily, by injections of whole blood.

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# SYPHILITIC CIRRHOSIS OF THE LIVER IN AN INFANT *

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In the course of my pediatric work at Leningrad, Dorpat, and at present at the recently founded university at Smolensk, I acquired a rich and varied clinical and pathologic experience in respect to newly born and young infants. From my observations during this work I am reporting a case of atrophic cirrhosis of the liver of syphilitic origin in a breast fed infant of 4 months. With this I am again citing some other forms of syphilitic cirrhosis, as well as my observations encountered in the course of melena neonatorum and of cardiac anomalies (not compatible with extra-uterine life) and a case of cirrhosis showing cysts of the liver (lymph angioma cysticum hepatis congenitum).[1]

Exhaustive search of the literature shows the excessive rarity of syphilitic cirrhosis of the liver at this age and particularly of the atrophic form.

The clinical characteristics, the pathologic anatomy and especially the accurate histologic pictures of the last form have made it possible to draw conclusions of a definite nature in one case.

## REPORT OF CASE

*History.*—A child, weighing 5,300 Gm., remained in the hospital ten days and succumbed to a grippal bronchopneumonia during the pandemic of grip in 1925-1926. During life a pronounced generalized icterus, a hard liver with an abdominal venous network (caput medusae), absence of ascites, voluminous spleen, nasal hemorrhages and intestinal mucous placques in the region of the anus were observed. The examination of the blood showed: red blood cells, 2,960,000; white blood cells, 28,200; poikilocytosis and anisocytosis. Examination of the white cells showed: neutrophils, 46 per cent; lymphocytes, 38 per cent; eosinophils, 3 per cent; mononuclears, 13 per cent. The Wassermann reaction was positive in both mother and infant; the Pirquet reaction was negative.

*Autopsy.*—The liver was hard, greenish and mottled. The fibrous tissue was developed to such a point that its quantity was almost equal to that of the parenchyma and formed white or grayish nodules between the lobules—cirrhose en masse; no gummas were found; there were many newly formed biliary ducts, and alteration of the reticulo-endothelial apparatus also was noted.

Cirrhosis of the liver of an atrophic nature, developing rapidly, presented the following characteristics:

1. The presence of icterus, which depended on the retention of bile and partially also on its absorption from the destroyed hepatic tissue.

* Received for publication, Feb. 7, 1927.

1. Joukovsky, V.: Arch. f. Kinderh. **50**:110, 1909.

2. A certain disproportion between the great destruction of the parenchyma and the marked development of the connective tissue with its abundance of cellular elements.

3. The rarity of the condition in a breast fed infant (a peculiarly rare occurrence).

4. Penetration of fibrous tissue into the lobules, which is commonly encountered in atrophic cirrhosis in adults but usually not to such an advanced degree.

# SANGUINEOUS LACRIMATION

## REPORT OF A CASE *

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Sanguineous lacrimation, or hemorrhage from the lacrimal gland, though rare, is not unknown. A review of the literature shows that the terms sanguineous lacrimation and bloody tears are frequently used synonymously, which is a mistake. Sanguineous lacrimation may produce blood tears, but not all cases of bloody tears are necessarily sanguineous lacrimation. The phenomenon has been known from antiquity, is most frequently found in young females and is not hereditary.

A brief review of the cases found on record after a careful search of the literature follows:

In 1581, Dodonaeus [1] briefly records his observations on a girl who, at the age of 16, had not menstruated; nature therefore attempted to rid itself of the excess blood through the eyes, since sanguineous drops which resembled tears frequently flowed from them.

Raigerus,[2] in 1755, reported the case of a boy, aged 15 months, who shed bloody tears on several occasions after having cried for some time. Examination of the eyes, cheeks and face did not reveal any abnormality. The child was of a tempestuous disposition, and the author judged that he had ruptured some capillary vessels in the angle of the eye which had furnished the drops of blood. He states that this symptom is not without example but that it is rare and cites cases reported by Forestus [3] and Hecksteterus [4]

Hasner,[5] in an article written in 1859, states that a distinction should be made between hemorrhages of the lacrimal gland and those of the conjunctiva, the former constituting true bloody lacrimation. He reports two cases, the first in a robust butcher, the result of a polypoid proliferation of the conjunctival fold with a slender pedicle, with complete recovery after removal of the polyp. The second occurred in a girl, aged 13, with daily recurring hemorrhages from the eyes. The absence of all pathologic changes in the conjunctival sacs, the eyeballs and the lids rendered it extremely probable that the source of the hemorrhage was in the lacrimal gland. The patient had

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* Received for publication, Dec. 23, 1926.

* From the pediatric outpatient department, Western Pennsylvania Hospital.

* Read before the Pittsburgh Academy of Medicine, Nov. 2, 1926.

1. Dodonaeus, R.: De Lachrymis sanguineis, Medicinalium observationum exempla rara, Coloniae, 1581.

2. Raigerus, C.: Sur les larmes de sang (On Bloody Tears), Collect. acad. de mem. Dijon **3**:303, 1755.

3. Forestus: Collect. acad. de mem. Dijon.

4. Hecksteterus: Collect. acad. de mem. Dijon.

5. Hasner: Bloody Lacrymation, Allg. Wien. med. Ztg. **4**:390 (Dec. 20) 1859.

not menstruated and was anemic. Two years later, Trantze[6] reported the same case as one of vicarious menstruation which entirely cleared up when the girl was 14, twenty days after she began to menstruate.

Damalix,[7] in 1882, reviewed the literature and, in addition to the cases cited above, mentioned those reported by Seger,[8] Lauzonus,[9] Cazelles,[10] Parrot[11] and Brun,[12] and described a case of bloody tears in a young woman who had been born of neuropathic parents and who had been so affected following a violent emotion. The condition continued for several months in spite of general and local treatment.

In 1887, Fieuzel[13] reported four cases of bloody tears; he did not see two of the patients, but they were reported to him by the parents. One of the other two cases occurred in a girl, aged 17, who showed a dark red, swollen conjunctiva, with desquamation of the epithelium in the superior culdesac; the other patient, a woman aged 35, showed a hard tumor at the level of the upper edge of the tarsal cartilage.

Cross,[14] in 1890, described a case in a woman, aged 21, observed for one and one-half years, who had frequently recurring bloody tears without, at any time, demonstrable lesions in the eyes. The condition seemed entirely independent of the menstrual periods, which were regular and normal. The author thought that the blood most likely came from the lacrimal gland, although no oozing from the duct could be discovered.

Konikow,[15] in 1916, recorded a case of severe epistaxis in which anterior and posterior tampons were inserted. A few minutes later bloody tears began to flow from the corresponding eye. Pressure on the nasal duct stopped the flow. This was a result of back pressure from the nasal cavity.

In 1923, Gabriélidès[16] reported two cases. The first occurred in a woman of 36 who was observed for four years. The blood appeared spontaneously and had no relation to crying or the menstrual periods. Examination showed the eyes, the urine and the blood to be normal. The second case was in a girl, aged 14. The menstrual periods began at the age of 13, and had appeared four times at intervals of from twenty to thirty days. They had ceased for four months, during which she shed bloody tears almost daily.

### AUTHOR'S CASE

To these I wish to add the following case: R. W., a girl, aged 6 months, was a full term baby, with a history of a normal birth. She weighed 7 pounds 8 ounces (3,401.9 Gm.) at birth and had been artificially fed since the first month of life. She was the fourth child of healthy parents, and had always been well and had made normal progress, weighing 13 pounds 6 ounces (6,066.8 Gm.) at 6 months of age. Two weeks before admission, the child developed a severe cold, with considerable nasal discharge and a slight cough.

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6. Trantze, C.: Blood Lachrymation, Allg. Wien. med. Ztg. **6**:4 (Jan. 1) 1861.

7. Damalix, A.: Des larmes de sang (Bloody Tears), Arch. d'oph. **2**:429 (Sept.) 1882.

8. Seger: Arch. d'ophth.

9. Lauzonus: Arch. d'ophth.

10. Cazelles: Arch. d'ophth.

11. Parrot: Arch. d'ophth.

12. Brun: Arch. d'ophth.

13. Fieuzel: Les larmes de sang (Bloody Tears), Bull. clin. nat. opht. de l'hop. d. quinze-vingts **5**:153 (July) 1887.

14. Cross, F. R.: Blood-Stained Tears, Tr. Ophth. Soc., U. Kingdom **11**: 242, 1890-1891.

15. Konikow, M. J.: Boston M. & S. J., Oct. 26, 1916.

16. Gabriélidès, A.: Tears of Blood, Ann. d'Ocul. **160**:705 (Sept.) 1923.

On several occasions during this time, when she cried especially hard the mother noticed that the tears were red and stained the linen. There was some fever during the duration of the cold, but the baby continued to take her feedings well.

Examination revealed a physically normal child, weighing 13 pounds 8 ounces (6,123.5 Gm.). There was considerable mucopurulent discharge from both sides of the nose and slight redness of the pharynx. After some difficulty, the child was induced to cry vigorously, and definitely blood stained tears flowed from both eyes. Previous to the crying no conjunctival inflammation could be discovered, and careful examination did not reveal any abnormality of the eyeballs or eyelids. A smear was taken of the bloody fluid which on staining was found to be loaded with red blood cells. Appropriate treatment was prescribed for the cold and boric acid wash for the eyes. The blood appeared several times during the next few days and entirely cleared up as the cold in the head improved. Since that time, frequent examinations under similar strain but without the coryza have not caused the condition to recur. The blood examination showed: red blood cells, 3,400,000; white blood cells, 6,400; hemoglobin, 80 per cent; the differential count showed: polymorphonuclears, 67; small lymphocytes, 25; large lymphocytes, 4; transitionals, 1; eosinophils, 1. The coagulation time was three minutes. Examination of the urine was negative.

## SUMMARY AND CONCLUSIONS

A summary of the etiologic factors concerned in the nineteen cases found in the literature shows: six cases associated with menstrual disturbances; three cases of emotional strain; one case of rupture of the capillary vessels of the eye; one case of conjunctivitis; one case of tumor of the eyelids; one case probably from the lacrimal gland; one case due to back pressure from the nasal cavity; five cases, cause not given.

I believe that the case reported is one of sanguineous lacrimation resulting from an acute inflammation of the lacrimal gland, associated with an upper respiratory infection. In support of this conclusion the following points are presented:

1. The sanguineous lacrimation appeared first in association with an acute condition of the upper respiratory tract.

2. It was present only when an extra demand was made on the lacrimal gland.

3. It was bilateral.

4. It subsided simultaneously with the clearing up of the upper respiratory condition.

5. There was an absence of any discoverable condition of the conjunctiva, eyelids or eyeballs to account for it.

6. The general condition of the child and the blood and urinary examinations conclusively ruled out blood dyscrasias and deficiency diseases.

# EFFECT OF POTENT PARATHYROID EXTRACT ON CALCIUM BALANCE IN INFANTS*

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In recent years a number of workers have used various methods of acid extraction to isolate from fresh parathyroid glands a substance, which, when given parenterally in adequate doses, produces a remarkable rise in the concentration of calcium in the blood serum. Collip and his associates have shown that the injection of a potent extract raised the concentration of serum calcium not only in parathyroidectomized dogs in whom the initial values were low, but also in intact dogs in whom the initial values were normal. Collip [1] has recently published a comprehensive review of this experimental work.

A few observers [2] have used such extracts, the potency of which had been proved in animals, in the treatment of both idiopathic and accidentally induced tetany in man. In all the reported cases the patients were relieved of clinical symptoms during the period of administration. Analyses of the blood showed that an increase in the concentration of the serum calcium invariably accompanied the clinical improvement.

This rapid increase in concentration of serum calcium resulting from injections of parathyroid extract may be ascribed (1) to an increased retention of exogenous calcium as a result of improved absorption, diminished excretion, or a combination of both factors (tendency toward positive balance), or (2) to mobilization of endogenous calcium either without any consequent loss to the body (stationary balance) or with overflow excretion in the urine and stools (tendency toward negative balance).

* Received for publication, Dec. 29, 1926.

* From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Collip, J. B.: Medicine **5**:1 (Feb.) 1926.

2. Collip, J. B., and Leitch, D.: Canad. M. A. J. **15**:59 (Jan.) 1925. Davidson, J. R.: ibid. **15**:803 (Aug.) 1925. Crile, G. W.: Endocrinology **9**:301, 1925. Snell, A. M.: Parathyroid Extract in Treatment of a Case of Tetany, J. A. M. A. **85**:1632 (Nov. 21) 1925. Lisser, H., and Shepardson, H. C.: Endocrinology **9**:383 (Sept.) 1925. Collip, J. B., and Blais: Medicine **5**:54 (Feb.) 1926. Petty, O. H.; Stoner, W. H., and Shaffer, H. W.: Report to the Philadelphia County Med. Soc., Oct. 28, 1925. Hoag, L. A., and Rivkin, H.: Treatment of Infantile Tetany with Parathyroid Extract, J. A. M. A. **86**:1343 (May 1) 1926.

The latter state, although eventually harmful, might be warranted over short periods of time when an elevation of serum calcium might insure relief from alarming symptoms.

Greenwald and Gross [3] have attempted to determine which of the foregoing sources suggested accounts for the increase in serum calcium. They placed three dogs on standard low-calcium diets and determined the urinary and fecal output of calcium and phosphorus in periods preceding and during the injection of a potent parathyroid extract. Since all three animals excreted more calcium and phosphorus in the test than in the control periods, the authors concluded that the extract mobilized the salts of these elements from the reserves of the body and that during this flooding of the circulation some of these salts were lost to the body through the urine and stools. They state:

> It should be clearly understood by those who attempt to use it (parathyroid extract) that the hypercalcemia it induces is not due to improved assimilation but is the cause of an increased loss of calcium. It is not to be used to promote calcium assimilation for only the contrary result is to be anticipated.

## PURPOSE

The present investigation was made in order to extend to human beings a study of the effect of parathyroid extract on calcium and phosphorus balance. A satisfactory idea of the assimilation of a salt can be obtained only from a knowledge of the relation of total output to total intake while on an adequate diet—a study of balance—as opposed to fluctuations in output while on a standard and probably inadequate intake. Since diseases leading to a state of hypocalcemia afford the most obvious indication for the therapeutic employment of parathyroid hormone, a study of its influence on the calcium balance in these, or closely related, disorders seemed to be of even more importance than a study of its effect on normal persons. Infants were studied because of their relatively great intake and retention of calcium and phosphorus and because of the frequency of disturbances in their assimilation of these elements, as found in rickets and idiopathic tetany.

## METHOD

One normal infant, four with rickets and two showing manifest tetany were studied. All the diets were selected to cover the caloric, protein and calcium requirements and in each case remained unchanged throughout the experimental periods. The infants with tetany were given diets of the same composition as those which they had received previous to their admission to the hospital, so that immediate studies might be made. The other patients were kept on the selected diets for several days before collections were started. The diets contained only foods which permitted accurate handling for analytical procedures (milk, farina, crackers and orange juice).

The excreta and samples of the food were collected in periods arranged so as to allow estimation of the calcium balance in (1) a normal fore-period of

3. Greenwald, Isador; and Gross, Joseph: J. Biol. Chem. **66**:217 (Nov.) 1925.

from three to six days' duration, when this was compatible with the withholding of treatment, (2) from one to three test periods varying from two to six days in duration, during which time potent parathyroid extracts[4] were injected subcutaneously at intervals of from six to twenty-four hours and (3) an after-period of from two to four days' duration, during which no treatment was given or a different therapeutic agent was used. The effect of the injections of parathyroid extract on the serum calcium and phosphorus was determined by analyses at suitable intervals.

Nurses trained in metabolism work were in attendance on the patients throughout the experiments. Special mattresses made possible the separate collection of urine and stools (except in the one female in case 5). The specimens of urine were collected under toluol in twenty-four hour divisions and pooled to correspond with the periods described. The delimitation of the specimens of stools was more difficult. The accomplishment of this was attempted by administering 0.2 Gm. of carmine with the first meal of each period, saving the first stained stool and continuing the collection up to, but not including, the specimen similarly marked by carmine administered immediately after the closing of the period. The rate of passage of this dye through the intestine was so variable in different periods in the same patient (from eight to twenty-four hours in one) that the extent of admixture with previous and subsequent feedings may have differed considerably. For this reason another method of delimitation, recommended by Greenwald and Gross,[5] was simultaneously employed in six of the seven patients. Throughout the experiment these infants received a constant daily amount (10 Gm.) of infusorial earth divided equally among the feedings. This procedure not only helped to secure regular, bulky stools, but also, in the degree to which it was eliminated as silicon dioxide in the stools, it acted as a check on the carmine demarcation of the periods, furnishing a basic rate of excretion with which to compare the rate of calcium and phosphorus output.

In some of the cases roentgenograms taken before and after the administration of parathyroid extract were examined for changes in the character and rapidity of calcification or for evidence of decalcification. It soon became apparent that this method was not sufficiently accurate to allow conclusions to be drawn from cases studied over short intervals.

## REPORT OF CASES

Case 1.—(Normal, except for underdevelopment). B. A., a white boy, aged 17 months, weighing 18½ pounds (8.3 Kg.) was admitted to the ward with a mild upper respiratory infection, from which he had completely recovered before his calcium and phosphorous balance was studied. Examination showed no physical signs of rickets or tetany, and roentgenograms of the radial and ulnar epiphyses showed normal structure of bones.

On the basis of the demarcation of stools by carmine this infant showed a distinct decrease in retention of calcium (table 1) during the four-day test-period in which the administration of 240 units[6] of parathyroid extract (7.22 units per kilogram per day) elevated his serum calcium from 9.1 to 15.7 mg. per 100 cc. In spite of this potential loss of calcium he remained in positive balance until the after-period. This aparently prolonged effect on the output of calcium may have been the result of persistent action of the hormone even

4. The extracts used were parathyroid extract (Collip), New and Nonofficial Remedies 1925, and Para-thor-mone, Eli Lily and Co.

5. Greenwald, Isador; and Gross, Joseph: J. Biol. Chem. **66**:185 (Nov.) 1925.

6. "A unit of potency has been provisionally defined as 1/100 of the amount of extract which will produce an average increase of 5 mg. in the blood serum calcium of normal dogs of approximately 20 kilos weight over a period of 15 hours." (Collip).

after the administration was discontinued, but there is also a possibility that it was due, in part at least, to the inclusion in the stools of more fecal material than properly belonged to this period. To permit an unexpected, early discharge from the ward the last stool had to be secured by means of a distilled water enema, which may have brought with it material representing food ingested

TABLE 1.—*Normal Infant (Case 1)*

| | Fore-Period 2/16-2/19 (3 Days) | | | Test Period 2/19-2/23 (4 Days) | | | After-Period 2/25-2/28 (3 Days) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.03* | 0.36* | .... | 0.14* | 0.51* | .... | 0.03* | 0.25* | .... |
| Stools | 0.78 | 0.42 | 6.22 | 0.80 | 0.43 | 6.69 | 1.05 | 0.59† | 6.67 |
| Total daily output | 0.81 | 0.78 | (62.2%) | 0.94 | 0.94 | (71.1%) | 1.08 | 0.84 | (66.7%) |
| Total daily intake | 1.04 | 0.91 | 10 | 1.02‡ | 0.87‡ | 9.41‡ | 1.06 | 0.91 | 10 |
| Daily balance | +0.23 | +0.13 | .... | +0.08 | —0.07 | .... | —0.02 | +0.07 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.125 | 0.067 | .... | 0.119 | 0.064 | .... | 0.157 | 0.088 | .... |
| Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § | | | | | | | | | |
| Daily average output of silicon dioxide | .... | .... | 6.54 | .... | .... | 6.54 | .... | .... | 6.54 |
| Theoretical daily total output | 0.85 | 0.80 | .... | 0.92 | 0.93 | .... | 1.06 | 0.83 | .... |
| Theoretical daily balance | +0.19 | +0.11 | .... | +0.10 | —0.06 | .... | 0.00 | +0.08 | .... |
| Remarks | | | | Parathyroid Extract | | | No treatment | | |
| | | | | Days: 2/19, 2/20, 2/21, 2/22 — Units: 60, 80, 60, 40 — 7.22 units per Kg. per day | | | | | |
| Mg. per 100 Cc. | Serum, 2/19 Calcium, 9.1 Phosphorus, 7.2 | | | Serum, 2/22 Calcium, 15.7 Phosphorus, 5.6 Serum, 2/23 Calcium, 15.5 Phosphorus, 4.9 | | | Serum, 2/28 Calcium, 9.3 | | |

* One slight urine loss.
† Stool secured by enema.
‡ A subtraction was made for the quantity found by analysis in a small amount of vomitus.
§ In this and the following tables calculations were made thus:

(a) Daily average output of silicon dioxide =

$$\frac{\text{Total silicon dioxide output in entire experiment}}{\text{Number of days in experiment}}$$

Example:

$$\frac{(6.22 \times 3) + (6.69 \times 4) + (6.67 \times 3)}{10 \text{ days}} = 6.54$$

(b) Theoretical daily stool output =
(Daily average output of silicon dioxide) × (Gm. per 1 Gm. silicon dioxide in stool)
Example:
Fore-period calcium: 6.54 × 0.125 = 0.82 Gm.

(c) Theoretical daily total output =
(Theoretical daily stool output) + (daily urine output)
Example:
Fore-period calcium: 0.82 Gm. + 0.03 Gm. = 0.85 Gm.

(d) Theoretical daily balance = (total daily intake) — (Theoretical daily total output)
Example:
Fore-period calcium: 1.04 — 0.85 = +0.19 Gm.

after the expiration of the after-period. This food was not accompanied by infusorial earth, so it was impossible to use the output of silicon dioxide as a true check on the rate of excretion of calcium. Proper segregation was attempted on the basis of carmine staining. There is general agreement in the trend shown by the figures secured by the two methods (table 1).

It is interesting to note that the parathyroid extract markedly increased the fraction of calcium excreted in the urine—from 3.7 per cent in the fore-period to 14.9 per cent in the test period—resulting in a proportional increase of 403 per cent.

Case 2 (Very mild rickets).—W. K., a fairly well nourished white boy, aged 11 months and weighing 17 3/16 pounds (7.8 Kg.) was admitted to the hospital for observation. Clinical and roentgenographic examinations revealed a mild grade of rickets undergoing healing. The serum phosphorus was 5.6 mg. per hundred cubic centimeters.

The administration of small doses of parathyroid extract to this infant (2.56 units per kilogram per day, a total of 100 units in five days) raised the concentration of calcium in his blood serum from 10.0 to 13.8 mg. per hundred

Table 2.—*Mild Rickets (Case 2)*

| | Fore-Period 6/22-6/28 (6 Days) | | | Test Period 6/29-7/4 (5 Days) | | | After-Period 7/6-7/12 (6 Days) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.01* | 0.33* | .... | 0.03* | 0.38* | .... | 0.27 | 0.39 | .... |
| Stools | 0.79 | 0.35 | 8.72 | 0.73 | 0.31 | 6.44 | 0.87 | 0.33 | 8.08 |
| Total daily output | 0.80 | 0.68 | (87.2%) | 0.76 | 0.69 | (64.4%) | 1.14 | 0.72 | (80.8%) |
| Total daily intake | 0.91 | 0.84 | 10 | 0.90 | 0.80 | 10 | 0.87 | 0.82 | 10 |
| Daily balance | +0.11 | +0.16 | .... | +0.14 | +0.11 | .... | −0.27 | +0.10 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.091 | 0.040 | .... | 0.113 | 0.048 | .... | 0.108 | 0.041 | .... |
| Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § | | | | | | | | | |
| Daily average output of silicon dioxide | .... | .... | 7.81 | .... | .... | 7.81 | .... | .... | 7.81 |
| Theoretical daily total output | 0.72 | 0.65 | .... | 0.92 | 0.76 | .... | 1.11 | 0.71 | .... |
| Theoretical daily balance | +0.19 | +0.19 | .... | −0.02 | +0.04 | .... | −0.24 | +0.11 | .... |
| Remarks | | | | Parathyroid Extract | | | No treatment | | |
| | | | | Days Units 6/29-7/4, 20 daily Total of 100 units, 2.56 units per Kg. per day | | | | | |
| Mg. per 100 Cc. | Serum, 6/16 Calcium, 9.6 Phosphorus, 5.6 | | | Serum, 7/3 Calcium, 12.4 Phosphorus, 5.1 | | | Serum, 7/12 Calcium, 10.8 Phosphorus, 5.5 | | |
| | Serum, 6/28 Calcium, 10.0 Phosphorus, 6.6 | | | Serum, 7/4 Calcium, 13.8 | | | | | |

* Very small urine losses, estimated and included in the calculations.
§ See footnote, table 1.

cubic centimeters. This rise was accompanied by a marked reduction in retention of calcium (table 2), which resulted in a slightly negative balance in the test period and which became even more evident in the after-period. These periods were separated by an interval of two days (last horizontal line in table 2). In this case the balances calculated according to the two methods for demarcation of the stools are not in agreement. The figures secured on the basis of excretions of infusorial earth are preferred to those based on the carmine marking for the following reason: since the percentage of recovery of infusorial earth was considerably less during the test period than it was during either of the others it seems reasonable to assume that the feces for this period (as separated by carmine) were incomplete and that part of the excreta from the intake during the test period was collected in the stools of the interval immediately following or during the after-period itself. This would partially explain the apparent reduction in the excretion of fecal calcium in the test-period and its sudden rise in the after-period.

As in case 1, the fraction of calcium excreted in the urine rose markedly during the experiment—from 1.3 per cent of the total in the fore-period to 23.7 per cent in the after-period—and there was a 2,700 per cent increase in the actual daily urinary output of calcium.

CASE 3 (Rickets).—S. V., a well nourished white boy, aged 8 months, weighed 16.5 pounds (7.4 Kg.) at the time of admission to the hospital. Whereas clinical examination revealed the bony changes characteristic of moderately severe rickets, roentgenograms showed striking rachitic lesions with evidence of healing already in progress (fig. 1).

This patient received parathyroid extract in varying doses continuously for twenty-five days (table 3). Balance studies were made in three test periods of three, three and four days' duration, respectively, during which the daily dosage of parathyroid extract was 5.44, 8.16 and 5.44 units per kilogram. The first two test periods included the initial six days of parathyroid administration;

Fig. 1 (case 3).—(March 18, 1926.) Roentgenogram of left wrist taken before the patient was given parathyroid extract. The radial and ulnar zones of provisional calcification show a degree of irregularity which is indicative of moderate rickets already undergoing some healing.

the third period comprised the final four days of treatment. The total amount of extract injected was 820 units in the twenty-five days. The effect on the level of serum calcium was negligible. Following the test periods the patient received intensive irradiations with the mercury vapor quartz lamp for seven days, during the last four of which balance studies were made.

The figures on the calcium balance based on demarcation by carmine show, during all the test periods, a tendency toward both a relative and an absolute loss of calcium from the body. In the second test period, however, the correctness of the division into periods by carmine is not verified by the figures on the excretion of silicon dioxide. Here, judging by the high percentage of recovery of infusorial earth, there appears to have been a certain amount of overlapping in the stools from the previous period, which, when corrected, brings the balance on the positive side. The loss of calcium from the body

TABLE 3.—*Rachitic Infant (Case 3)*

| | Fore-Period 3/22-3/26 (4 Days) | | | Test Period 1 3/26-3/29 (3 Days) | | | Test Period 2 3/29-4/1 (3 Days) | | | Interval-Period 4/1-4/15 (14 Days) | Test Period 3 4/15-4/19 (4 Days) | | | Ultra Violet Light Period 4/21-4/25 (4 Days) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.02 | 0.27 | .... | 0.04 | 0.39 | .... | 0.03 | 0.34 | .... | ..... | 0.34 | 0.33 | .... | 0.01 | 0.36 | .... |
| Stools | 0.43 | 0.18 | 8.01 | 0.56 | 0.23 | 7.34 | 0.59 | 0.24 | 8.79 | ..... | 0.75 | 0.28 | 8.37 | 0.43 | 0.17 | 6.02 |
| Total daily output | 0.45 | 0.45 | (80.1%) | 0.60 | 0.62 | (73.4%) | 0.62 | 0.58 | (87.9%) | ..... | 1.09 | 0.61 | (83.7%) | 0.44 | 0.53 | (60.2%) |
| Total daily intake* | 0.46 | 0.46 | 10 | 0.59 | 0.52 | 10 | 0.61 | 0.54 | 10 | ..... | 0.76 | 0.73 | 10 | 0.72 | 0.50 | 10 |
| Daily balance | +0.01 | +0.01 | .... | −0.01 | −0.10 | .... | −0.01 | −0.04 | .... | ..... | −0.33 | +0.12 | .... | +0.28 | −0.03 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.054 | 0.022 | .... | 0.076 | 0.031 | .... | 0.067 | 0.027 | .... | ..... | 0.09 | 0.033 | .... | 0.071 | 0.028 | .... |
| Daily average output of silicon dioxide† | .... | .... | 8.04 | .... | .... | 8.04 | .... | .... | 8.04 | Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § ..... | .... | .... | 7.19 | .... | .... | 7.19 |
| Theoretical daily total output | 0.45 | 0.45 | .... | 0.65 | 0.64 | .... | 0.57 | 0.56 | .... | ..... | 0.98 | 0.57 | .... | 0.52 | 0.56 | .... |
| Theoretical daily balance | +0.01 | +0.01 | .... | −0.06 | −0.12 | .... | +0.04 | −0.02 | .... | ..... | −0.22 | +0.16 | .... | +0.20 | −0.06 | .... |
| Remarks | | | | Parathyroid Extract: Days 3/27, 3/28, 3/29; Units 40, 40, 40; 5.44 units per Kg. per day | | | Parathyroid Extract: Days 3/30, 3/31, 4/1; Units 40, 80, 60; 8.16 units per Kg. per day | | | Parathyroid Extract: 360 units in 14 days at 12 hr. intervals | Parathyroid Extract: Days 4/16, 4/17, 4/18, 4/19; Units 40, 40, 40, 40; 5.44 units per Kg. per day | | | Ultraviolet Light at 50 Cm.: 4/19-4/21, 16 min.; 4/21-4/25, 50 min. | | |
| Mg. per 100 Cc. | Serum, 3/26: Calcium, 8.2; Phosphorus, 3.3 | | | Serum, 3/29: Calcium, 8.2; Phosphorus, 3.0 | | | Serum, 4/1: Calcium, 9.0; Phosphorus, 2.1 | | | | Serum, 4/17: Calcium, 8.2; Phosphorus, 2.9 | | | | | |

* The variable daily intake of calcium and phosphorus was dependent on refusals of food in the first three periods.

† Because of the long time intervals between the second and third test periods the daily average excretion of infusorial earth during the first three periods was calculated separately from the average for the last two periods.

§ See footnote, table 1.

Fig. 2 (case 3).—(April 6, 1926.) Roentgenogram of left wrist taken after the patient had received 380 units of parathyroid extract in the course of ten days. The zones of provisional calcification appear essentially the same as they did before the extract was administered (fig. 1).

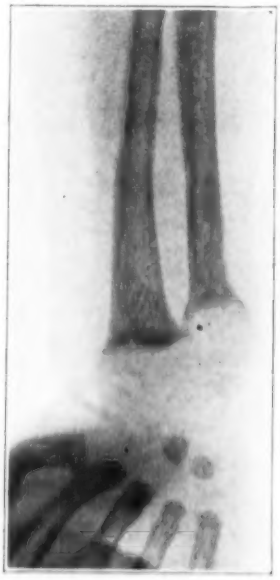

Fig. 3 (case 3).—(April 19, 1926.) At this time the patient had received 750 units of parathyroid extract in twenty-three days. There is a greater decrease in the density of the cortex of the bone and zones of provisional calcification than can apparently be accounted for by differences in the technic of radiography.

during the last four of the twenty-five days in the test period was striking. In the after-period with ultraviolet radiation, the calcium balance returned sharply to the positive side, the retention exceeding that in the fore-period.

Roentgenograms taken at intervals of from five to seven days during the administration of parathyroid extract showed a state of slight and practically stationary healing at the zone of provisional calcification (figs. 2 and 3). At the end of the succeeding seventeen days, during the first seven of which he received ultraviolet radiations daily, there was evidence of distinct acceleration in the healing process at the zone of provisional calcification (fig. 4). No significant change in the density of the cortex of the bone could be detected.

The urinary fraction of the total output of calcium was raised under the influence of parathyroid extract from 4.4 per cent in the fore-period to 31.2 per cent in the third test period, then fell abruptly to 2.3 per cent in the period of ultraviolet radiation.

Fig. 4 (case 3).—(May 5, 1926). Roentgenogram of left wrist taken ten days after the last of a series of seven daily ultraviolet irradiations (sixty-six minutes total exposure at a distance of 50 cm.). This treatment produced a distinct acceleration of calcification in a period of time considerably shorter than that during which the administration of parathyroid extract caused no recognizable change.

Case 4 (Mild rickets).—W. B., a white boy, aged 4 months, weighed 13.5 pounds (6.1 Kg.) when admitted to the ward for an upper respiratory infection. Clinical and roentgenographic signs of mild active rickets were present, although the concentration of serum phosphorus was normal (5.9 mg. per hundred cubic centimeters). All signs of acute infection had disappeared before the study was begun.

The effect of parathyroid extract on the calcium balance was studied in two test periods of five days' and six days' duration, respectively, separated by an interval of two days. In the first period (table 4) a daily dose of 2.46 units of extract per kilogram caused a negligible rise in the concentration of serum calcium and a moderate tendency toward loss of calcium from the body. In the second test period the dose of extract was increased to 6.14 units per kilo-

TABLE 4.—*Mild Rickets (Case 4)*

| | Fore-Period 6/27-7/3 (6 Days) | | | Test Period 1 7/5-7/10 (5 Days) | | | Test Period 2 7/12-7/18 (6 Days) | | | After-Period 7/20-7/25 (5 Days) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.001 | 0.35 | .... | 0.03 | 0.38 | .... | 0.08 | 0.45 | .... | 0.02 | 0.30 | .... |
| Stools | 0.42 | 0.18 | 4.02 | 0.81 | 0.15 | 5.73 | 0.59 | 0.16 | 4.88 | 0.70 | 0.25 | 4.80 |
| Total daily output | 0.42 | 0.53 | (40.2%) | 0.84 | 0.53 | (57.3%) | 0.67 | 0.61 | (48.8%) | 0.72 | 0.55 | (48.0%) |
| Total daily intake * | 0.84 | 0.72 | 10 | 0.88 | 0.73 | 10 | 0.96 | 0.76 | 10 | 0.97 | 0.75 | 10 |
| Daily balance | +0.42 | +0.20 | .... | +0.04 | +0.20 | .... | +0.29 | +0.15 | .... | +0.25 | +0.20 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.104 | 0.045 | .... | 0.141 | 0.023 | .... | 0.121 | 0.033 | .... | 0.146 | 0.052 | .... |
| | Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § | | | | | | | | | | | |
| Daily average output of silicon dioxide | .... | .... | 4.75 | .... | .... | 4.75 | .... | .... | 4.75 | .... | .... | 4.75 |
| Theoretical daily total output | 0.56 | 0.56 | .... | 0.70 | 0.50 | .... | 0.65 | 0.61 | .... | 0.71 | 0.55 | .... |
| Theoretical daily balance | +0.34 | +0.17 | .... | +0.18 | +0.23 | .... | +0.31 | +0.15 | .... | +0.26 | +0.20 | .... |
| Remarks | | | | Parathyroid Extract | | | Parathyroid Extract | | | No treatment | | |
| | | | | 7/5-7/10, 15 units daily<br>Total of 75 units<br>2.46 units per Kg. per day | | | Days / Units<br>7/13 30<br>7/14 45<br>7/15 45<br>7/16 45<br>7/17 45<br>7/18 15<br>6.14 units per Kg. per day for six days | | | | | |
| Mg. per 100 Cc. | Serum, 6/29<br>Calcium, 9.2<br>Phosphorus, 5.9<br>Serum, 7/3<br>Calcium, 9.5 | | | Serum, 7/7<br>Calcium, 9.8<br>Phosphorus, 6.5<br>Serum, 7/9<br>Calcium, 10.3<br>Phosphorus, 6.4 | | | Serum, 7/14<br>Calcium, 11.2<br>Phosphorus, 6.1<br>Serum, 7/18<br>Calcium, 9.6<br>Phosphorus, 4.5 | | | Serum, 7/25<br>Calcium, 9.3<br>Phosphorus, 4.7 | | |

* The variation in the figures for total daily intake was larger in this case than usual. It is not sufficiently great, however, to explain away the differences in balance.

§ See footnote, table 1.

gram daily, but even this amount did not cause any constant or marked elevation of concentration of serum calcium. The retention of calcium in this period showed a return toward the level as seen in the fore-period, a tendency which was also evident in an after-period without any treatment. The changes in retention were not as striking in this case as in the previous ones.

The fraction of the total calcium excreted in the urine rose from 0.2 per cent in the fore-period to 3.6 per cent and 11.9 per cent, respectively, in the first and second test periods.

Case 5 (Rachitic dwarf).—G. L., a white girl, aged 3 years, was admitted to the hospital because of marked undernutrition and delayed development. Although artificially fed from birth, she had thrived up to the age of 9 months, at which time she had had a severe attack of pneumonia. The slow convalescence from this illness necessitated a residence in the hospital for five months. During this period she had lost the ability to stand, and had never regained it. At the time of admision she was 30 inches (76.2 cm.) tall and

Table 5.—*Rachitic Dwarf (Case 5)*

| | Fore-Period 1/31-2/4 (4 Days) | | Test Period 2/4-2/10 (6 Days) | | After-Period 2/14-2/19 (5 Days) | |
|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Calcium, Gm. | Phosphorus, Gm. | Calcium, Gm. | Phosphorus, Gm. |
| Total daily output of urine and stools | 0.98 | 0.80 | 0.46 | 0.76 | 0.50* | 0.56* |
| Total daily intake | 1.21 | 1.16 | 1.21 | 1.11 | 1.21 | 1.02 |
| Daily balance | +0.23 | +0.36 | +0.75 | +0.35 | +0.71 | +0.46 |
| Remarks | Periods divided by enemas; none at beginning of fore-period | | Parathyroid Extract | | Ultraviolet Light at 50 Cm. | |
| | | | About 200 units in 6 days at 8 hour intervals; 3.9 units per Kg. per day | | 2/10-2/14: 48 min. 2/14-2/19: 76 min. | |
| Mg. per 100 Cc. | Serum, 2/3 Calcium, 7.4 Phosphorus, 2.5 | | Serum, 2/6 Calcium, 7.7 Phosphorus, 2.8 | | Serum, 2/19 Calcium, 8.7 Phosphorus, 3.9 | |
| | | | Serum, 2/7 Calcium, 7.4 Phosphorus, 4.0 | | | |
| | | | Serum, 2/8 Calcium, 7.8 Phosphorus, 3.9 | | | |

* Two small losses of urine.

weighed only 19 pounds (8.6 Kg.). There were both physical and roentgenographic signs of rachitic changes in the bones. The outstanding features were the underdevelopment, atony and hypofunction of all the skeletal muscles.

This patient was a female so that separate collections of the urine and stools were not attempted. She was the first patient studied in this series, and the methods of delimiting the periods as described above had not yet been elaborated. The results were so striking, however, that it is difficult to explain away their significance on the basis of errors in collection.

The data as presented in table 5 show a marked improvement in retention of calcium during the administration of about 200 units of parathyroid extract[7] in the course of six days (3.9 units per kilogram per day). This amount of the extract caused no distinct elevation of the concentration of serum calcium[8]

7. This extract was furnished through the courtesy of Parke, Davis and Company.

8. This same extract caused a rise of serum calcium concentration in a patient with infantile tetany and in a normal infant.

above the original low level of 7.4 to 7.8 mg. per hundred cubic centimeters. The high positive balance induced by the extract was not quite maintained during an after-period of intensive ultraviolet therapy. The great difference between the fore-period and test period was certainly due to some extent to the method of collection of stools in this case. After the patient had been on a constant diet for several days the collections of urine and stools for the fore-period were begun. At the end of this four-day period the entire contents of the lower bowel were obtained by an enema. It is therefore certain that these stools represented the ingested food not only of the four-day period, but possibly of five or even six days, if the initial stool of the fore-period were partly derived from pre-period food. Assuming even this high estimate of six days to be more nearly correct, the revised proportional output for four days would have been 2.61 Gm. of calcium ($0.98 \times 4 \times 4/6$), resulting in a daily positive balance of 0.56 Gm. Even this figure is less than the 0.75 Gm. and 0.71 Gm. positive

TABLE 6.—*Infantile Tetany (Case 6)*

| | Fore-Period 2/16-2/19 (2⅔ Days) | | | Test Period 2/19-2/23 (4 Days) | | | After-Period 3/1-3/4 (3 Days) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.003* | 0.32 | .... | 0.007 | 0.35 | .... | 0.003* | 0.20* | .... |
| Stools | 0.93 | 0.39 | 8.79 | 0.77 | 0.34 | 8.52 | 0.80 | 0.37 | 8.26 |
| Total daily output | 0.93 | 0.71 | (90.4%) | 0.78 | 0.69 | (86.5%) | 0.80 | 0.66 | (82.0%) |
| Total daily intake | 0.90 | 0.81 | 9.73 | 0.88 | 0.82 | 9.86 | 0.83 | 0.74 | 10 |
| Daily balance | −0.03 | +0.10 | .... | +0.10 | +0.13 | .... | +0.03 | +0.08 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.106 | 0.044 | .... | 0.090 | 0.040 | .... | 0.097 | 0.045 | .... |
| Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § | | | | | | | | | |
| Daily average output of silicon dioxide | .... | .... | 8.52 | .... | .... | 8.52 | .... | .... | 8.52 |
| Theoretical daily total output | 0.90 | 0.70 | .... | 0.78 | 0.69 | .... | 0.83 | 0.67 | .... |
| Theoretical daily balance | 0.00 | +0.11 | .... | +0.10 | +0.13 | .... | 0.00 | +0.07 | .... |
| Remarks | | | | Parathyroid Extract | | | No treatment | | |

| Days | Units |
|---|---|
| 2/20 | 80 |
| 2/21 | 80 |
| 2/22 | 70 |
| 2/23 | 40 |

7.63 units per Kg. per day

| | | | |
|---|---|---|---|
| Mg. per 100 Cc. | Serum, 2/16<br>Calcium, 7.1<br>Phosphorus, 3.9 | Serum, 2/22<br>Calcium, 8.8<br>Phosphorus, 3.7 | Serum, 3/2<br>Calcium, 7.8<br>Phosphorus, 2.6 |
| | Serum, 2/19<br>Calcium, 7.9<br>Phosphorus, 3.7 | | |

* One voiding lost.
§ See footnote, table 1.

daily balances of the test period and after-period (table 5) in which the separations of stools was probably accomplished with a fair degree of accuracy by enemas at both the beginning and end of the periods.

CASE 6 (Infantile tetany).—P. R., an overnourished colored boy, aged 9 months, weighing 19½ pounds (8.85 Kg.), was brought to the hospital on Feb. 16, 1926, during the course of a generalized convulsion. No physical signs of mechanical hyperirritability (Chvostek, peroneal reflex or Trousseau) could be elicited, but the finding of hyperirritability to the galvanic current and the presence of a serum calcium concentration of 7.1 mg. per hundred cubic centimeters confirmed the suspected diagnosis of infantile tetany. In addition, a roentgenogram of the radius and ulna showed distinct evidence of rickets.

The calcium balance was studied during a fore-period of two and two-thirds days without any treatment, and it was found that the output was practically equal to the intake (table 6). During the succeeding four days the patient

was given 270 units of parathyroid extract (7.63 units per kilogram per day). This relatively large dose caused only a slight rise in the concentration of serum calcium—from 7.9 mg. to 8.8 mg. per hundred cubic centimeters. In this period calcium was retained, the balance changing to the positive side, both on the basis of carmine-marking and excretion of infusorial earth. After an interval of several days without treatment the retention of calcium had decreased, the intake and output again being almost equal.

The amount of calcium excreted in the urine was almost negligible throughout the experiment, and the apparent increase in the urinary fraction in the test period falls within the error of the method.

Case 7 (Infantile tetany).—V. P., a white boy, weighing 15 pounds (6.8 Kg.), aged 5½ months, was brought to the hospital on April 19, 1926, as a normal patient. The examination at admission revealed a distinct "crow," a facial phenomenon (Chvostek) and a suggestive Trousseau sign. The diagnosis of

Table 7.—*Infantile Tetany (Case 7)*

| | Fore-Period 4/19-4/22 (2⅔ Days) | | | Test Period 4/22-4/26 (4 Days) | | |
|---|---|---|---|---|---|---|
| | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. | Calcium, Gm. | Phosphorus, Gm. | Silicon Dioxide, Gm. |
| Urine | 0.000 | 0.23 | .... | 0.001 | 0.27 | .... |
| Stools | 0.60 | 0.26 | 6.76 | 0.60 | 0.23 | 7.90 |
| Total daily output | 0.60 | 0.49 | (70.2%) | 0.60 | 0.50 | (79.0%) |
| Total daily intake | 0.66 | 0.51 | 9.63 | 0.62 | 0.52 | 10 |
| Daily balance | +0.06 | +0.02 | .... | +0.02 | +0.02 | .... |
| Gm. per 1 Gm. silicon dioxide in stool output | 0.089 | 0.038 | .... | 0.076 | 0.029 | .... |
| Calculated on Basis of Same Excretion of Silicon Dioxide in All Periods § | | | | | | |
| Daily average output of silicon dioxide | .... | .... | 7.44 | .... | .... | 7.44 |
| Theoretical daily total output | 0.66 | 0.52 | .... | 0.57 | 0.49 | .... |
| Theoretical daily balance | 0.00 | −0.01 | .... | +0.05 | +0.03 | .... |
| Remarks | | | | Parathyroid Extract | | |
| | | | | Days: 4/23 — Units: 160 | | |
| | | | | 4/24 — 80 | | |
| | | | | 4/25 — 120 | | |
| | | | | 4/26 — 60 | | |
| | | | | 15.5 units per Kg. per day | | |
| Mg. per 100 Cc. | Serum, 4/19 | | | Serum, 4/24 | | |
| | Calcium, 4.4 | | | Calcium, 6.4 | | |
| | Phosphorus, 6.7 | | | Phosphorus, 5.4 | | |
| | Serum, 4/21 | | | Serum, 4/26 | | |
| | Calcium, 4.9 | | | Calcium, 6.5 | | |
| | Phosphorus, 7.2 | | | Phosphorus, 5.3 | | |

§ See footnote, table 1.

infantile tetany was verified by demonstrating a cathodal opening contraction with slightly less than 5 milliamperes of galvanic current, and a concentration of serum calcium of 4.4 mg. per hundred cubic centimeters. In addition he showed clinical and roentgenologic signs of moderate rickets.

In a fore-period study of two and two-thirds days without treatment he showed practically no retention of calcium (table 7). During the four-day test-period 420 units of parathyroid extract (15.5 units per kilogram per day) were administered, and this amount caused an elevation of serum calcium from 4.9 to 6.5 mg. per hundred cubic centimeters. The effect on the calcium balance was slight. On the basis of carmine separation of the stools there was an apparent decrease in the retention, but the data calculated from the excretion of infusorial earth showed an insignificant increase in retention. Although the latter figures are considered more reliable, the change in either direction is so small that it falls within the error of the method. The significant point in the

results secured in the study of the two cases of infantile tetany seems to lie not so much in the moderately increased retention of calcium in case 6 and the very slightly improved retention in case 7, as it does in the fact that parathyroid extract did not cause a definite loss of calcium from the body.

It is interesting to note that in case 7 the fraction of calcium excreted in the urine was small in both periods, lying beyond the limit of accurate analysis.

## COMMENT

The reaction of individual patients to parathyroid extract varies tremendously and depends on factors which cannot at present be evaluated. This diversity in response, together with the small number of cases studied, precludes any too general statements.

The effect of parathyroid extract on the calcium balance in infants is apparently not universally harmful, as might have been expected on the basis of the experiments on animals we have cited. In only four of the seven cases studied was the retention of calcium unfavorably influenced, and in these the extract appears to have produced a loss in body calcium rather than a reduction in the amount absorbed from the intestine, since the excretion of calcium in the urine invariably rose, in both an absolute and a relative manner. Three patients showed no decrease in the retention of calcium. The two with infantile tetany showed a slight tendency toward improved retention of calcium while receiving parathyroid extract. As has been pointed out, this increase in retained calcium in case 7 was small enough to be within the error of the method, while in case 6 the increase was unmistakable. Throughout the experiments the amount of calcium excreted in the urine of both patients was so small that slight changes which might have occurred in the separate periods could not be accurately analyzed. The results in the rachitic dwarf (case 5) showing improved retention of calcium during the administration of parathyroid extract cannot be unqualifiedly accepted, but are so striking that their significance seems to be beyond doubt.

It may be significant that the three patients in whom parathyroid extract apparently produced an improved retention of calcium were the ones showing the most marked clinical evidences of disturbed calcium metabolism. In these the concentration of serum calcium was initially low and was only slightly increased (never to normal) by doses of extract which in normal infants would ordinarily cause a much more marked elevation. If the action of parathyroid extract consists, as Greenwald and Gross [3] suggest, in increasing the serum solubility of the calcium salts of the bones, then it is conceivable that in patients with initially low concentration of serum calcium in the blood a slight accretion from the bones would still not bring the concentration to the point at which loss from the body through the urine and stools would result. On the other hand, the increased concentration of serum calcium might, by mass action, stimulate bone deposition of calcium so that the solvent action of the extract might be partially self-limiting through the estab-

lishment of an equilibrium. In this connection it may be mentioned that in two patients (cases 2 and 4) in whom parathyroid extract produced moderate rises in serum calcium above the initial normal levels, and in whom these increases were comparable to those produced in the patients in cases 6 and 7, who had initially low serum calcium values, there was a tendency for calcium to be lost from the body.

The improved retention produced in cases 6 and 7 was not sufficiently striking to suggest the use of parathyroid extract for its ultimate effect on the calcium balance, even in cases with initially low serum calcium concentrations.

## LABORATORY PROCEDURES

The specimens of blood serum were analyzed in duplicate, using the method of Kramer and Tisdall[9] for calcium and that of Tisdall[10] for inorganic phosphorus.

Specimens of milk, urine and stool were preserved with chloroform and toluol and kept on ice during collection and until analyzed. The specimens of food consisted of equal aliquot fractions of the retained intake for each day. Any rejection was carefully measured and subtracted. The specimens of urine were acidified in the collection bottles after measuring, then pooled quantitatively and diluted to a convenient volume. The stools were transferred quantitatively to a large porcelain dish, strongly acidified and steamed for several hours to split calcium from its insoluble soap and phosphate forms. This procedure resulted in an extremely even suspension, which was forced through a fine-mesh sieve and then diluted to a convenient volume. The aliquot fractions for analysis were drawn up with a pipet during vigorous stirring of the suspension.

All specimens were oxidized in triplicate, using at least 100 cc. of milk, from 200 to 300 cc. of urine and from one-thirtieth to one-fifteenth of the total stool suspension. If the results showed more than 5 per cent total variation (2.5 per cent mean deviation), the analyses were repeated until constant results were secured. Oxidation was accomplished by boiling with sulphuric acid and nitric acid over an open flame. It was carried to the point of complete disappearance of all sediment (except silicon dioxide in specimens of stools). The mixture was then diluted, neutralized and slightly reacidified before filtering through double-acid-washed paper. Residues of infusorial earth thus retained were repeatedly washed with weak hydrochloric acid, transferred in the filter paper and strongly ignited to constant weight. The filtrate and washings were made up to definite volume.

The calcium in the filtrates was analyzed by a modified McCrudden method[11] using a faint pink with methyl red to indicate the optimum $p_H$ for the precipitation of calcium oxalate. The precipitation mixture was heated and allowed to stand over night. Filtration was on a hard double-acid-washed paper. The ammonia-washed and acid-dissolved calcium oxalate was titrated with tenth normal or five-hundredths normal potassium permanganate, except for some of the urines which required one-hundredth normal potassium permanganate.

The total phosphorus was determined in the same fully oxidized digestion mixtures by comparing a suitably selected aliquot fraction with 1 mg. of standard phosphorus by Brigg's[12] modification of the Bell-Doisy method. Only those readings were accepted which fell within 25 per cent of the setting of the standard. Full acceptance of these figures may not be advisable in view of the possibilities of

9. Kramer, Benjamin; and Tisdall, F. F.: J. Biol. Chem. **47**:475 (Aug.) 1921.
10. Tisdall, F. F.: J. Biol. Chem. **50**:329 (Feb.) 1922.
11. McCrudden, F. H.: J. Biol. Chem. **7**:83, 1910; ibid. **10**:187, 1911.
12. Briggs, A. P.: J. Biol. Chem. **53**:13 (May) 1922; ibid. **59**:255 (March) 1924.

error in this method, as recently emphasized by Stanford and Wheatley[13] and Roe, Irish and Boyd.[14] They believe the most important sources of error to be: oxidation at temperatures above 200 C., color development in the presence of high concentrations of sodium sulphate, at variable acidities, and in the presence of sufficient excess of molybdic acid and hydroquinone to result in some color from this system independent of the phosphorus content.

## SUMMARY

1. The influence of potent parathyroid extracts on the calcium (and total phosphorus) balance was studied in seven infants: one normal, four rachitic and two with infantile tetany. The results secured in the test periods with parathyroid extract were controlled by fore-period and after-period studies without the extract. In every case the diets provided an adequate amount of calcium and phosphorus.

2. One normal infant and three infants with rickets showed distinct diminution of calcium retention during the periods in which parathyroid extract was administered. The decrease did not bear a constant relation to the dosage nor to its effect on the level of serum calcium. In these cases the extract caused both an absolute and a proportional increase in the urinary excretion of calcium.

3. One patient with rickets (case 3) was given parathyroid extract daily for twenty-five days without producing recognizable roentgenologic evidence of either calcium removal or deposition in the radius and ulna.

4. Two patients with infantile tetany (cases 6 and 7) showed a slight tendency toward increased retention of calcium during the periods in which parathyroid extract was administered. One rachitic patient (case 5) with striking signs of disturbed calcium metabolism showed a more marked increase in the retention of calcium. In these cases the concentration of serum calcium was initially low and was not markedly raised by the extract (never reaching normal levels). The urine in all periods contained such minute quantities of calcium that significant changes could not be detected by the method employed.

5. The total phosphorus method employed is under criticism, so the data relating to balance, which was obtained by its use, are not discussed. It may be noted that a relative and an absolute increase in urinary phosphorus invariably followed the administration of parathyroid extract.

6. Even though the influence of potent parathyroid extracts on the balance of calcium was not found to be uniformly unfavorable, its administration for any purpose other than immediate, temporary elevation of serum calcium should still be considered an experimental and not a routine clinical procedure.

161 West Sixty-First Street.

13. Stanford, R. V., and Wheatley, A. H.: Biochem. J. **19**:697, 1925.

14. Roe, J. H.; Irish, O. J., and Boyd, J. I.: J. Biol. Chem. **67**:579 (March) 1925.

# ANURIA OF SEVEN DAYS' DURATION IN A CHILD WITH SCARLET FEVER *

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## CASE REPORT

*History.*—A girl, white, aged 3 years and 6 months, had always been in excellent health. There had been no known exposure to scarlet fever. On Feb. 22, 1925, she had an acute rhinopharyngitis which was followed by otitis media; paracentesis of the drum of the left ear was performed, and there was a purulent discharge from the ear for a few days. The ear had healed completely by March 5.

On the evening of March 14, the child complained of feeling sick. On March 16, a definite diagnosis of scarlet fever was made. During the acute stage of the disease the patient was quite ill; she had a high fever (from 103 to 105 F.), extensive eruption and a moderately severe sore throat. The angina was sufficient to cause desquamation of the mucous membranes, with resultant white patches over the ulcerated areas on the tonsils and pharynx. As a precaution, therefore, even though the throat cultures were negative for Klebs-Loeffler bacilli, 10,000 units of diphtheria antitoxin were injected intramuscularly. The acute symptoms of the scarlet fever lasted about one week; on March 23, the temperature had become normal, the eruption had disappeared and the condition of the throat had become much better.

In the meantime a new and disturbing condition presented itself. About noon on March 20, the child voided urine containing albumin and blood. Following this, there was complete anuria for seven days and six hours. The nurse was certain that the child had not passed any urine, and catheterization yielded none. In spite of the improved clinical condition, which at first somewhat obscured the significance of the anuria, intensive treatment seemed advisable, and the child was brought to the contagious department of the Cincinnati General Hospital.

During the period of the anuria, the patient was never unconscious or delirious. At times she was irritable and at other times quiet and complacent. She answered questions and cooperated during the physical examinations; she asked for her toys, but would play with them for only a short time. She picked at her lips, which were excoriated and bled easily. The withdrawal of food and later of fluid did not seem to disturb her. There were no signs of uremia; neither persistent vomiting, drowsiness nor convulsive twitching occurred. The most disturbing symptom was abdominal distention which was usually successfully relieved by the passage of a stomach tube. Toward the end of the period of anuria there were frequent movements of the bowel, probably induced by an irritation of the lower bowel from retention enemas of sodium bicarbonate.

*Examination.*—On physical examination slight edema of the lower extremities was found, and dulness in the flanks indicated a small amount of ascitic fluid. Occasional scattered râles were heard throughout both lungs. The heart was not enlarged, but a faint blowing systolic murmur developed over the pulmonary area. Fever was not present during the last four days of the anuria.

*Treatment and Course.*—The treatment consisted of intravenous injections of hypertonic solutions, given with the view of reducing the edema, which it was felt must be present in the tissue of the kidney and must be the cause of the anuria. The details of the injections are given in table 1.

No fluids were given by mouth during this treatment, but several retention enemas of 4 per cent sodium bicarbonate were given.

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* Received for publication, Dec. 31, 1926.

Observations of the blood pressure were made frequently during the intravenous injections. On March 26, the blood pressure averaged 93 systolic and 55 diastolic; on the morning of March 27, it was 102 systolic and 70 diastolic. Following the injections of the glucose solutions, a surprising fall in diastolic blood pressure was noticed. On March 27, at 4:30 p. m., it was 105 systolic and 0 diastolic, and at 6:30 p. m., 98 systolic and 40 diastolic; on March 28, 8:00 a. m., 76 systolic and 0 diastolic; on March 29, a. m., 100 systolic and 0 diastolic; on March 30, in the forenoon, 120 systolic and 50 diastolic, and in the afternoon, 104 systolic and 0 diastolic; on March 31 and on subsequent days, the diastolic blood pressure was always above 50 mm.

Urine was first obtained at 6 p. m., March 27, by catheterization. The child voided for the first time on March 29. Further intravenous injections were not given after that time, and it was fortunate none were necessary, as the supply of suitable veins was about exhausted.

After March 29, the child voided urine at least three or four times daily in amounts which were estimated to total 200 cc. per day. The exact quantity was uncertain, as the child did not cooperate well and usually wet the bed. The first urine obtained was of a dark grayish brown color, somewhat cloudy and slightly acid, and it contained a moderate amount of albumin, many red and

TABLE 1.—*Intravenous Therapy to Overcome Anuria*

| Day | Date | Time | Solution, per Cent | Amount | Urine |
|---|---|---|---|---|---|
| Friday..... | March 20 | 12 n. | ..... | ..... | Hematuria and Albuminuria |
| Wednesday.... | March 25 | 12 n. | Glucose..... 10% | 150 cc. | |
| Thursday..... | March 26 | 10 a.m. | Magnesium sulphate... 2%<br>Calcium chloride..... 0.2% | 90 cc. | |
| | | 5 p.m. | Magnesium sulphate... 2%<br>Calcium chloride..... 0.2% | 200 cc. | No urine |
| Friday..... | March 27 | 4 p.m. | Glucose..... 40% | 230 cc. | |
| | | 6 p.m. | ..... | ..... | 1 cc. |
| | | 9 p.m. | Glucose..... 40% | 150 cc. | ..... |
| Saturday..... | March 28 | 8 a.m. | ..... | ..... | 4 cc. |
| | | 10 a.m. | Glucose..... 40% | 60 cc. | ..... |
| | | 4 p.m. | Glucose..... 40%<br>Sodium chloride..... 2% | 150 cc. | ..... |
| | | 9 p.m. | ..... | ..... | 6 cc. |
| | | 10 p.m. | Glucose..... 2%<br>Sodium chloride..... 2% | 305 cc. | ..... |
| Sunday..... | March 29 | ..... | ..... | ..... | Voided 3 times |

white blood cells, and hyaline and granular casts. For the next three weeks, the urine continued to be of much the same appearance; the reaction was sometimes alkaline, and sometimes acid; the relative amount of albumin and the number of casts diminished, but the red and white blood cells persisted. Sugar was never found, and acetone was present on only one occasion.

On March 28, the child developed fever and a serum eruption, obviously the result of the antitoxin given nine days previously. For several days following, there was considerable improvement. The patient's appetite was good, and the outlook seemed good. On March 31, a setback occurred in the development of an otitis media in the right ear, and mild bronchitis. The child's appetite became finicky and vomiting was frequent during the following ten days; however, the general trend seemed toward improvement until April 11. On this date an otitis media also developed in the left ear, and a pleuritic friction rub was noticed at the right base. The child gradually became worse, and shortly before her death on April 18 a diagnosis of empyema in the right side of the chest was made.

The status of the function of the kidney was followed by frequent analyses of the nonprotein nitrogen constituents of the blood. The results of these blood chemical studies are given in table 2.

The maximum retention was reached on March 30 and 31; from that time until April 11, the function of the kidney gradually improved; the further infection then led to a rise in the urea, uric acid and creatinine content of the blood. Several attempts were made to do a phenolsulphonphthalein function test, but these were unsuccessful because of difficulty in collecting the urine; apparently dye was not excreted.

*Necropsy.*—Examination of the kidneys showed that they were large and congested. Their weight was 265 and 270 Gm., respectively, about three times the normal size for the patient's age. Many grayish triangular areas were noticed on cut section, indicating infarcts. The microscopic sections showed two processes, (*a*) edema, dilatation of the tubules and glomeruli, atrophy of the cells of the tubules and casts—indicating convalescence from an acute nephritis, apparently of toxic origin from the scarlet fever; (*b*) a marked invasion of polymorphonuclear leukocytes, apparently due to septicemia occurring late in the disease (fig. 1). The liver showed marked fatty change (fig. 3). Bronchopneumonia was present as well as pleuritis and empyema in the lower part of the right side of the chest. We are indebted to Dr. J. Ganim and Dr. R. S. Austin for assistance in these examinations.

TABLE 2.—*Blood Chemistry*

| Date | Urea Nitrogen, Mg. per 100 Cc. | Uric Acid, Mg. per 100 Cc. | Creatinine, Mg. per 100 Cc. | Sugar, per Cent | Carbon Dioxide Content, per Cent by Volume |
|---|---|---|---|---|---|
| March 26 | 75 | 11.0 | 8.2 | .15 | .. |
| March 28 | 90 | .... | 8.3 | ... | .. |
| March 30 | 113 | .... | 9.6 | .15 | .. |
| March 31 | 122 | 19.0 | ... | ... | .. |
| April 1 | 113 | 15.8 | 8.5 | ... | .. |
| April 2 | 107 | .... | 6.6 | ... | .. |
| April 4 | 96 | 11.1 | 6.6 | ... | .. |
| April 6 | 103 | 8.0 | 5.7 | ... | .. |
| April 8 | 83 | 7.4 | 5.3 | ... | .. |
| April 9 | 76 | 6.4 | 6.6 | ... | .. |
| April 11 | 60 | 3.9 | 4.8 | ... | .. |
| April 13 | 107 | .... | 6.4 | ... | .. |
| April 14 | 121 | 8.1 | 7.5 | ... | 67 |
| April 16 | 103 | 11.8 | 6.8 | ... | .. |

*Summary.*—The outstanding features in this case may be summarized under the following divisions:

1. Nephritis appeared on the sixth day of severe scarlet fever.

2. Anuria lasted seven and one-fourth days and was without symptoms of uremia.

3. The patient was treated for anuria by means of hypertonic (dehydrating) solutions, which incidentally caused a collapsing pulse and low diastolic blood pressure.

4. The function of the kidney was being restored until a streptococcus septicemia caused further injury to the kidney (suppurative nephritis). This late scarlatinal septicemia resulted in otitis media and empyema, and finally in the death of the patient.

## COMMENT

Scarlatinal nephritis seldom appears before the tenth day of the disease; in occasional cases it has occurred earlier. Jubel-Renoy [1] reports a case of nephritis, with anuria of seven days' duration and a fatal termi-

1. Dieulafoy, G.: A Textbook of Medicine, New York, D. Appleton & Co., 1911, p. 1590.

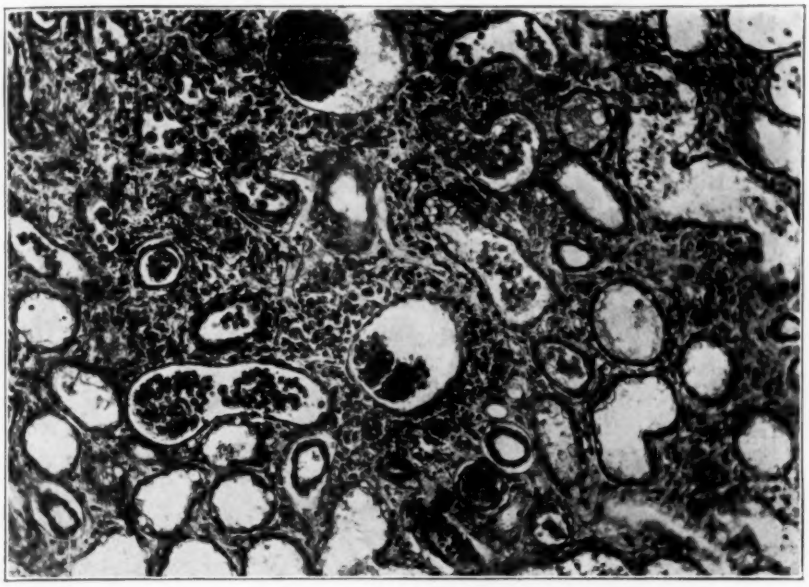

Fig. 1.—A section of the kidney of the patient, showing dilation of tubules, atrophy of cells of tubules and invasion by leukocytes.

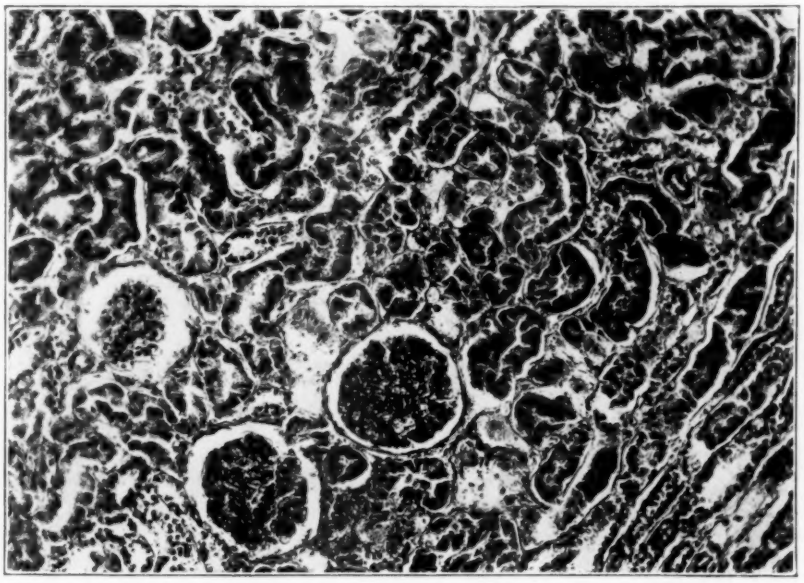

Fig. 2.—Section of the normal kidney for comparison.

nation in the early stages of scarlet fever. In the present case, involvement of the kidney was not the febrile albuminuria so often seen during the first week of the disease; there is a possibility that the infection from February 22 to March 5 may have been a factor in causing the nephritis, which was made more severe by the concurrent scarlet fever.

Anuria in scarlatinal nephritis is rare. In Dunham's [2] case, the anuria lasted fifty-one hours, with recovery; urine was voided ten hours following intravenous injection of a solution containing 3 per cent sodium chloride and 2 per cent sodium carbonate. Ker,[3] in his textbook,

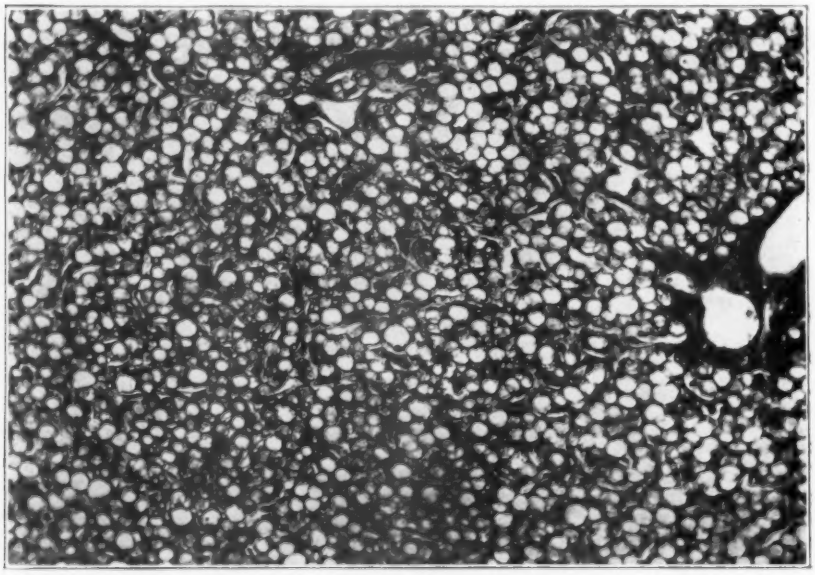

Fig. 3.—Section of the liver showing fatty change.

recounts one case in which complete suppression of urine continued for five days, with recovery of the patient. Wilson [4] reports a similar case in which anuria lasted nine days, the patient dying.

Pisano [5] reports the case of a child, aged 3, who had a light attack of scarlet fever and developed nephritis ten days later; for ten days urinary excretion was nil, sweating was abundant, there was constipation, and the

2. Fischer, M.: Oedema and Nephritis, New York, John Wiley & Son, 1921, p. 701.

3. Ker, C. B.: Infectious Diseases, New York, Oxford University Press, 1920, p. 117.

4. Wilson, J. C.: Infectious Diseases, New York, D. Appleton & Co., 1905, p. 397.

5. Pisano, G.: Caso straordinario di anuria completa durata dieci giorni; guarigione, Gior. di med. mil., Roma **24**:431, 1876.

patient vomited only when fluids were forced. There was no edema; the child was sometimes excited and sometimes sleepy. When urine was again passed, it was reddish, acid and contained albumin, numerous epithelial cells, casts and altered blood cells. The child recovered rapidly. Northrop [6] reports a case of a child who had anuria of five days' duration following scarlet fever; the child had edema of the face and extremities and marked ascites; there were no symptoms of uremia. As in our case, diphtheria antitoxin had been given. The child recovered.

Harding [7] reports complete suppression of urine during the course of a scarlatinal nephritis in a boy, aged 12; the child was unconscious, having previously lost vision and hearing. An operation was performed (decapsulation of both kidneys); the kidneys were as large as adult kidneys, tense and congested; "on removal of the capsule the blood fairly boiled from the kidney surface, showing the very high pressure it was under." The child voided 24 ounces (710 cc.) of urine during the twenty-four hours following the operation, and recovered rapidly, being discharged from the hospital in eighteen days.

There are several cases of postscarlatinal anuria in the literature in which the urine before and after the anuria seemed clear and normal and contained no albumin or blood. Willau's [8] patient, a boy, aged 9, had anuria of two days' duration, and died during a convulsion. Whitelaw's [9] patient, a boy, aged 8, had anuria for twenty-five days, except that he passed 2 ounces (0.13 Gm.) of urine on the thirteenth day; he recovered. Clough's [10] patient had intermittent anuria over forty-five days, passing 91 ounces (2,830 Gm.) of urine in that time.

When anuria occurs in acute nephritis, the failure to excrete water is probably due to edema of the kidneys. Martin Fischer in his writings has advised the use of hypertonic solutions to reduce this edema and permit excretion of fluid. Dr. Fischer personally made several valuable suggestions in the treatment of this patient. It may be mentioned that decapsulation of the kidney to relieve the tension was being seriously considered as a last resort to overcome the anuria.

We recognize a bare possibility that the diphtheria antitoxin may have played some rôle in the causation of the anuria.

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# GONOCOCCUS ARTHRITIS IN INFANCY

## A CLINICAL STUDY OF FORTY-FOUR CASES *

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PHILADELPHIA

Outbreaks of gonococcus arthritis in the new-born are exceedingly rare in hospitals. A search of the archives reveals no contemporary record of such occurrences, although prior to the introduction of antiseptic midwifery, the disease known as puerperal fever of the new-born, with joint complications probably of gonococcic origin, was prevalent. L. Emmett Holt, in 1905, reported twenty-six cases of gonococcus arthritis collected over a period of years from the Babies Hospital, New York. This was the largest number of cases of this disease from a single institution then on record. Incidentally, it might be of interest to note that fourteen of these infants died of the disease.

In view of the rarity of this condition, I desire to place on record an experience with a remarkable outbreak of gonococcus arthritis in a large maternity hospital in Philadelphia. This epidemic aroused a neighborhood against the institution, caused its temporary shutdown as a maternity hospital and its transformation into an orthopedic hospital, and led to a wide variety of diagnoses until the correct one was made and the disturbance traced to its probable source.

The period covered was from the latter days of August to the end of September, 1924, when 182 infants were born in the hospital. Sixty-seven of these were infected, fifty-three of which presented joint complications; the others presented infections of the mucous membrane only. Forty-four of the former were readmitted to this hospital and to the Mt. Sinai Hospital when they were 5 weeks of age.

Although this communication is chiefly concerned with the orthopedic phases of the disease, a brief review of the early clinical manifestations might be apropos.

All of the infected infants came from the same ward. Those cared for on a separate floor during this period were free from the taint, the source of which was either a negro laundress or a parturient patient who were in the institution during the latter part of August, 1924. The contagion was probably introduced into the nursery by an infant who had some of the infected discharges on its body. It was then disseminated unknowingly by the nurses to the other infants through contaminated rectal thermometers, wash basins or laundry.

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The rectum is indicated as the most likely portal of entry because a number of male and female infants had purulent rectal discharges, ischiorectal abscesses and positive rectal smears. The infection was conveyed through the abdominal lymphatics to the blood stream and thence metastasized to the joints.

### CLINICAL MANIFESTATIONS

*Prodromal Stage.*—When these infants were 8 or 9 days old, the following symptoms were observed: elevation of temperature, which ranged between 99 and 102 F.; toxic rashes distributed over the body or extremities; swollen fingers or toes and superficial abscesses in various parts of the body. Little attention was paid to these symptoms. No rectal or vaginal discharges were observed during this period. A day or two after their discharge from the hospital, which was usually on the eleventh day, many of the infants were quite ill; they cried when handled and did not nurse well. Investigation showed numerous swollen joints, purulent discharges from the vagina, and diarrheas with stools purulent in character. Diagnostic perplexities regarding the nature of the illness were general. A striking illustration is the following:

Baby Z., a girl, was discharged on the eleventh day with a temperature of 100 F. and a swollen index finger; two days later, a profuse vaginal discharge was noted by the mother, also an apparently paralyzed and painful left lower extremity. A physician diagnosed the case infantile paralysis; another thought she had a fractured femur, because the upper part of the thigh was swollen and sensitive. The roentgen ray revealed a dislocation of the left hip. The correct diagnosis was finally established in the Philadelphia General Hospital when she was 4 weeks of age.

The first clue regarding the nature of the epidemic was observed in a male infant 2 weeks old on or about Sept. 18, 1924. The left knee was swollen and fluctuated on pressure. On aspiration, 5 cc. of serosanguineous fluid was withdrawn; smears and culture showed the gonococci. This infant was promptly discharged from the hospital. Two days later, a female infant 6 days old with gonorrheal ophthalmia was discovered. This infant was referred to an eye dispensary. On the same day a number of infants that had been delivered several weeks previously were seen in the postnatal clinic with swellings of the joints and vulvovaginitis. It was then definitely realized that gonorrhea was on the rampage in this institution, and immediate action was taken by the board of managers to stamp it out. From that period to Jan. 1, 1925, the hospital was barred to maternity cases. The social service department began a round up of infected infants for the maternity hospital and Mt. Sinai Hospital. On October 12, there were twenty-two infants in the former institution and eight male infants in a small isolated ward at Mt. Sinai Hospital. The other

infants were admitted within the next few weeks. Of the sixty-seven patients located by the social service department, twenty-seven were males and forty females, and of the forty-four that came under my care, twenty-one were males and twenty-three females. Every female infant had vulvovaginitis; five males and three females had gonorrheal proctitis and one female infant had gonorrheal ophthalmia.

### HOSPITALIZATION

The length of time that these infants were kept in the hospitals was from one to three months; they were discharged when the acute clinical manifestations had abated and smears had become negative. During this period the general manifestations were those of a septic nature, with irregular elevations of temperature ranging from 99 to 103, which became normal on subsidence of the infection. Severe febrile reactions were observed in six cases. These were probably due to secondary infections, one of which may be mentioned—a male infant, aged 6 weeks, with a double knee infection. Two days after an arthrotomy and the institution of Willems' treatment, the temperature rose to 108, preceded by a convulsion. It came down to 103 in several hours, but continued at this level for ten days, after which it gradually declined to normal. A secondary invasion with *Staphylococcus aureus* was the cause of the severe reaction.

The nutrition of most of these infants was remarkably well preserved, the local severity of the pyemic process being in strong contrast with the mild constitutional symptoms. They apparently seemed to thrive in spite of the disease. A few infants, whose resistance was poor, showed marked wasting, prostration and anemia. There were no demonstrable visceral complications. The heart, lungs and kidneys at no time during the course of the infection presented signs of involvement.

The blood picture showed a moderate leukocytosis, ranging between 11,760 and 27,800; the erythrocytes numbered between 2 and 4 million and hemoglobin between 40 and 80 per cent. The differential count showed the following variations: polymorphonuclear cells, from 40 to 70 per cent; small lymphocytes, from 30 to 50 per cent; large mononuclears, from 2 to 4 per cent. One blood culture was positive ten days after incubation in a male infant with polyarthritis. In the other cases, these studies gave negative results. The gonococcic fixation test was employed in eight cases, and in one was positive. Urine from females showed traces of albumin, many pus cells and gonococci. No gonococci were found in the urine of males. Bacteriologic studies of aspirated joint exudates revealed the gonococci early in the course of the disease. Subsequent studies failed to disclose these organisms. Mixed infection with other organisms were occasionally reported.

COMPLICATIONS IN THE JOINTS

The complications in the joints were the most interesting symptoms of the epidemic. The total number of infected joints was 136, excluding the spine, which was probably involved in six cases; a single joint was involved in ten cases, and two or more joints in thirty-four cases; the largest number of joints involved in an infant was eleven.

Fig. 1.—Male infant, aged 7 weeks, gonococcus polyarthritis. Eight joints were involved. This infant had suppurative arthritis of the left elbow and right ankle, pathologic dislocation of the left hip, pseudoparalysis of the left lower extremity and left wrist drop.

Fig. 2.—Same infant as in figure 2, with Thomas hip splint applied to correct the distortion and immobilize the left hip joint. The left elbow and right ankle have been incised and drained.

Involvements that were not strictly articular but that were misinterpreted at first as such were the superficial abscesses observed on a number of ankle and wrist joints in eight infants; in this connection may also be mentioned several cases of tenosynovitis of the flexor tendons of the fingers that resulted in destruction and loss of function in two cases.

Tables 1 and 2 indicate the extent of the infection.

The local reactions were striking. The skin was glazed, violaceous and hot to the touch. The contours of the joints were obliterated by a marked periarticular edema; the soft tissues were tumefied and of a "woodeny" resistance to palpation. Motion was markedly restricted by intense muscular spasm. Distortions were striking. In the hip joints, for instance, both thighs were rigidly flexed on the abdomen; the buttock was swollen and indurated and the spine kyphotic or scoliotic. The involved knees were globular in contour and were fixed in flexion by spasm of the hamstrings. The suprapatellar bursae were

TABLE 1.—*Extent of the Infection*

| Number of Infants | Number of Joints |
|---|---|
| 10 | 1 |
| 15 | 2 |
| 9 | 3 |
| 2 | 4 |
| 2 | 5 |
| 1 | 6 |
| 3 | 7 |
| 2 | 8 |
| 1 | 11 |
| Total | 136 |

TABLE 2.—*The Order, Frequency and Side Affected*

| | | Number of Infections | Number of Infants | Side Involved | | |
|---|---|---|---|---|---|---|
| | | | | Right | Left | Both |
| 1 | Wrists | 25 | 22 | 6 | 13 | 3 |
| 2 | Knees | 23 | 18 | 5 | 8 | 5 |
| 3 | Shoulders | 16 | 15 | 3 | 11 | 1 |
| 4 | Ankles | 18 | 16 | 9 | 5 | 2 |
| 5 | Toes | 16 | 10 | .. | .. | .. |
| 6 | Fingers | 14 | 12 | .. | .. | .. |
| 7 | Hips | 12 | 11 | 7 | 3 | 1 |
| 8 | Elbows | 9 | 8 | 4 | 3 | 1 |
| 9 | Tarsals | 3 | 2 | 1 | .. | 1 |
| | Total | 136 | | | | |

invariably involved and distended with fluid, which was serosanguineous, serofibrinous or purulent in character. The elbows were fusiform in shape and partially flexed. A marked tumefaction and swelling of the palm of the hand with a wrist drop accompanied all involvements of the wrist joints.

Pathologically, the following classification of reactions was observed: periarthritis, seventy-five joints (54.8 per cent); suppurative arthritis, forty-five joints (33.3 per cent); nonpurulent synovitis, sixteen joints (11.8 per cent).

The first group was characterized by an intense exudative inflammation affecting the periarticular tissues, viz., the muscles, tendons, ligaments, etc. When these tissues were incised, bleeding was profuse.

The deeper layers were markedly edematous, blanched or pearly gray in color. Stringy or flocculent collections of pus were observed between the joint capsules and overlying tissues and between muscular planes. Diagnostic joint puncture in these cases invariably resulted in dry taps.

In the second group, purulent collections, located by aspiration or arthrotomy, were observed in the large bursal sacs in relation to the shoulder and knee. The pus in these instances was liquid in consistency

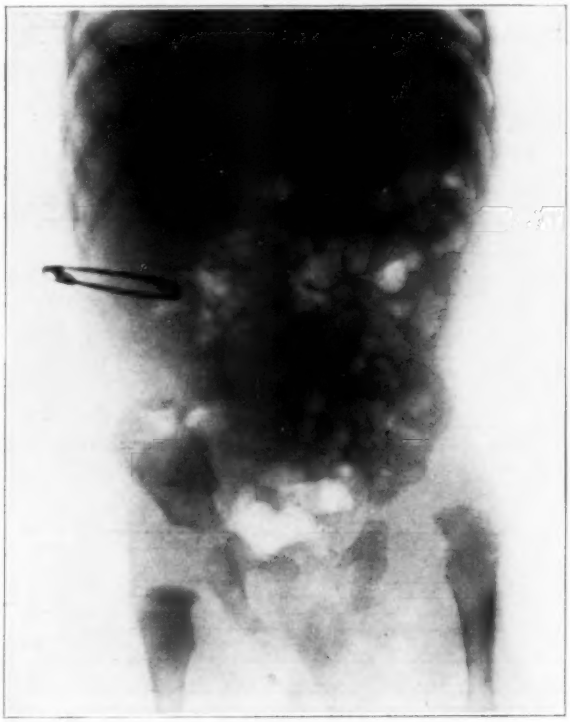

Fig. 3.—Gonococcus arthritis of the left hip, showing pathologic dislocation three weeks after onset of infection.

and was white or green. In the smaller joints, as the toe, elbow, ankle and wrist, the exudate was flaky or stringy in character and small in amount.

The last group, chiefly noted in the cases showing involvement of the knee, presented an acute exudative inflammation of the capsular and synovial lining of these joints. On aspiration, these collections were turbid or dirty yellow and occasionally bloody. Reaccumulations after aspiration were frequent in all of these cases. Resolution was tardy; hyperplasia of the periarticular tissues and mild flexion contractures were the sequelae.

Flaccid palsies, due to infiltration and edema of the peripheral nerve trunks in relation to the involved joints, were frequently observed. The brachial and lumbosacral plexuses were implicated to a greater or lesser degree in involvement of the shoulder and hip. The extremities were flail; muscular atrophy was pronounced, and reflexes were diminished. These symptoms mislead many physicians during the prodromal stage of the disease, the cases being mistaken for poliomyelitis or birth palsies. Symptoms referable to the central nervous

Fig. 4.—The left hip joint of the child shown in figure 3 at 22 months of age. The poorly defined capital epiphysis and shallow acetabulum should be noted. A closed reduction has been attempted, but without success.

system were observed in one female infant with polyarthritis and vulvovaginitis. The case simulated poliomyelitis in a striking manner; the extremities, back and abdomen were flaccid; muscular atrophy was progressive and the reflexes diminished. For eight months following the onset of the disease, this child was unable to hold its head up voluntarily or sit erect. It is highly probable that the spinal accessory nucleus was involved through invasion by the gonococcus or its toxin. Recovery was slow but progressive, and at the end of a year the child made a complete recovery.

BONE MANIFESTATIONS

The roentgen ray was freely employed from time to time to detect bone complications. Osteomyelitic foci within the shafts of the long bones, pathologic dislocations of the hip, retardation in appearance and abnormal development of the epiphyses and destructive changes in the acetabulae of infected hip joints were found in eighteen cases. The gonococcus was chiefly responsible for these infections of the bones, although it is probable that other pyogenic organisms might have been contributory causes. Central areas of osseus absorption were observed in the upper end of the humerus in two cases and in the upper end of the ulna in another case. The symptoms of these complications were severe, but no trephining was deemed advisable. Spontaneous resolution occurred in the cases.

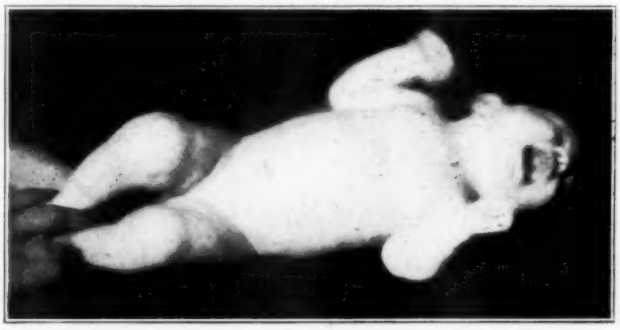

Fig. 5.—Female infant, aged 6 weeks, with suppurative gonococcus arthritis of the right knee. The joint has been incised and drained. The contour and size of this joint should be noted. At 1 year of age the appearance and function were normal, with negative roentgen-ray observations.

SPINAL CURVATURES

Special mention might be made regarding the spinal curvatures accompaning the involvements of the hip joints. These invariably were to the right or left, depending on the side affected, viz., in rightsided involvements, the curvature was to the left and vice versa. In cases involving both hips, rigid angular kyphoses were observed, the apex being at the lumbodorsal junction. These curvatures, induced by spasmodic action of the iliopsoas muscles on the infantile spine, were gradually corrected by casts. With the subsidence of the inflammation of the hip joint or joints, there was complete restoration of the spine to normal.

SEQUELAE

Mild contractures of the joints, soft tissue hyperplasia, residual foot and wrist drops and dislocations of the hips, were the sequelae noted in most of the cases after abatement of the acute inflammatory process in

the joints. These conditions persisted for a variable period of time, but under treatment complete functional restoration was obtained in all but the dislocations of the hips. Ankylosis, a common terminal effect in adult gonococcus arthritis, was not observed in any of the cases. This is a singular occurrence, gonococcus arthritis being one of the most destructive of the diseases of the joints, particularly if it is of the suppurative variety. The reason for so little damage to the joints in infancy may be explained by the natural resistance of the infantile joints, which are largely composed of cartilage, the greater reparative properties of the young periarticular tissues and perhaps by the treatment.

Dislocations of the hip joints were undoubtedly the most disastrous complications of the epidemic, permanently crippling most of these children. These dislocations occurred spontaneously shortly after the inception of the local infection. Spontaneous reduction occurred only

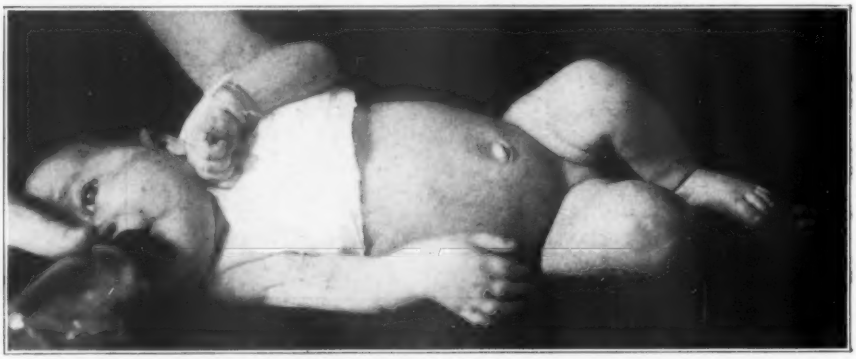

Fig. 6.—Female infant, aged 8 weeks, with three joints involved—left shoulder, right wrist and right knee. The subdeltoid bursa of the left shoulder has been incised and drained for suppurative bursitis. The size and contour of the right knee and the well nourished appearance of this infant should be noted. There was complete recovery at 16 months of age.

in one instance, in an infant 6 weeks of age in which a rightsided involvement was present. There were twelve dislocations in four males and eight females, one being a bilateral and eleven unilateral luxations. The chief predisposing cause was undoubtedly the rudimentary structure of the infantile hip joint with its shallow, poorly developed acetabulae and immature ligaments. The exciting factor was the increased intra-articular tension brought about by muscle spasm and the presence of inflammatory exudates within the joint cavity. These cases were recognized early by the roentgen ray, which showed an upward and backward displacement on the dorsum of the ilium. Serial roentgen-ray studies, taken from time to time, have shown profound changes in the shape of the femoral head and neck and erosion of the superior borders of the acetabulum. Ossification of the capital epiphyses

was delayed. In two cases, the epiphyseal cartilages were completely destroyed. In the majority of the cases the roentgen-ray appearance of these hip joints resembled, in a striking fashion, the picture of Perthe's disease, namely, flattening and fragmentation of the femoral head and distortion of the femoral neck. Of course, these changes were observed as the children grew older. Clinically, the following symptoms were noted: shortening, ranging between one-fourth and one-half inch, restricted mobility and a limp when the children began to walk.

### TREATMENT

During the acute stage of the epidemic, the members of the staff of the maternity hospital were all concerned in treating these infants. In this communication, I shall only consider the treatment of the complications in the joints, leaving the other manifestations (vulvovaginitis, proctitis, ophthalmia, etc.) to those associated with me.

Fig. 7.—Female infant, aged 7 weeks, with five joints involved. The right-sided wrist drop and the infection in the right shoulder and right elbow joints should be noted. The plaster cast has been applied to the right leg for involvement of the ankle joint. There was complete restoration of function at 14 months of age.

When I was first called on the scene, conditions were chaotic. Owing to the multiplicity and the progressiveness of metastases of the joints, each joint being a surgical problem, one can realize the difficulties that were encountered. The first thing that was done, during the acute stage, was to allay pain in the joints by protecting them against motion and jarring. These infants had to be handled frequently when nursing or when local vaginal treatments were administered, and at these times they experienced considerable pain and suffering. Whenever practical, all inflamed joints were immobilized in metal or plaster of Paris splints. The latter were difficult to apply at this early age, and before the proper technic was learned their application entailed a great amount of labor. Frequent soiling and softening of the casts would irritate the skin and make the infants uncomfortable, thus necessitating frequent changes.

Another handicap was the fact that the nursing staff was inexperienced in treating such cases. Difficulties, which at first appeared insurmountable, were finally conquered within about two weeks. With better team work and a perfection in the application of plaster of Paris, control of the situation was obtained. After considerable experimentation with metal, wooden and plaster splints, the metal and wood were discarded in cases involving the knees and hips, because they were difficult to keep

Fig. 8.—Female infant, aged 8 weeks, with three joints infected—right hip, right wrist and left ankle. Spinal curvature to the left and pathologic dislocation of the right hip joint are present. The type of cast employed is to correct the spinal distortion and immobilize the infected joints.

in place and produced a great deal of irritation. These joints, whether single or multiple, were immobilized in double plaster of Paris spicas, reaching from the nipple to the toes, in other words, completely fixing the lower half of the body. These plasters were widely cut so as to expose the lower abdomen, genitals and buttock; the limbs were in extreme abduction, which permitted vaginal treatments without soiling.

I might mention that the ordinary diaper was not used. Instead, large gauze pads were employed to collect the discharges and stools. Altogether, eighty-four casts of this type were employed in the two and one-half months that these infants were in the hospital. The marked relief of pain and the ease with which the infants could be handled without disturbing the sensitive joints can be definitely attributed to the perfect fixation that these casts assured. Deformities of the spine and hip and flexion contractures of the knee were gradually corrected by these appliances. Fenestrae in the casts were made over the knees when aspirations were employed.

Regarding splintage of the joints of the upper extremities, padded metal splints were employed in wrist and elbow joints. The shoulders could not be adequately immobilized. These had to be treated surgically

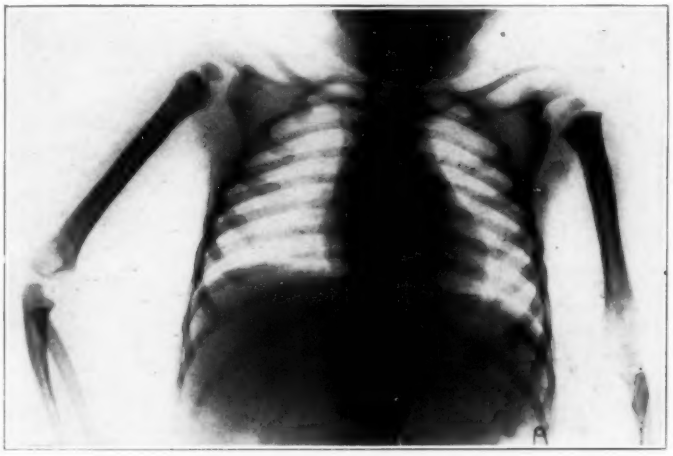

Fig. 9.—Gonococcus arthritis of the left shoulder in a child, aged 20 months, the infection occurring shortly after birth. The fragmentation and retarded growth of the upper humeral epiphysis as compared with the right side should be noted. The upper half of the diaphysis is thicker than the left, and at the epiphyseal line the end is broad and convexed. The left shaft is shorter than the right by 0.5 cm.

(aspiration, incision and drainage) or by local physiotherapeutic measures. The ankle joints were immobilized in plaster, reaching from the toes to the knee. The smaller joints (fingers and toes) could not be immobilized but were treated either surgically or by local applications.

### ASPIRATIONS AND ARTHROTOMIES

Intra-articular exudates were removed by either aspirations or incision and drainage of the joints. The total number of such surgical procedures was sixty-eight, forty-four aspirations and twenty-four incisions. The joints most frequently aspirated were the knees, puncture

usually being made into the suprapatellar bursae, in which the collections were found. The quantity of fluid withdrawn was from 4 to 10 cc. Reaccumulations were frequent, and aspirations were repeated in from three to five day intervals. Refill of the joint cavities after aspiration was less frequent in limbs fixed in plaster than in those in which no fixation was employed. Joints were incised and drained when diagnostic puncture or other physical signs indicated local suppuration. Following operation, the joint was covered by copious gauze dressings, which were kept moist with sterile physiologic sodium chloride solution; the joint was kept warm under an incandescent lamp. No drains were used, but

Fig. 10.—Gonococcus arthritis of right wrist at 18 months of age. Onset of the disease shortly after birth. Two centers of ossification of the carpals are observed in the right wrist as compared with three in the normal side.

at each dressing the operative wounds were opened and the joint irrigated with warm boric acid solution. The results obtained in these cases were indeed gratifying, damage to the joints being practically nil. Supplemented later by diathermy, complete function was obtained.

### DIATHERMY

Beginning in the acute stage and subsequently continued for almost eight months, diathermy treatments were applied to the large joints—hip, knee, shoulder, etc. The current employed was 200 milliamperes,

and the length of the treatment was from ten to fifteen minutes. Diathermy, a newer one of the physical agents in the treatment of this infection, hastened absorption of the products of inflammation. That the heat generated within deeper tissues might be bactericidal to the gonococcus is suggested by the significant observation; namely, the repeatedly negative smears from the joints shortly after the institution of this form of therapy.

### VACCINES

Twenty-three infants were treated with autogenous and stock vaccines. After a month's trial, this treatment was discontinued, because no apparent beneficial results were noted, either in checking the infections of the mucous membrane or the metastases to the joints. It is highly probable that the organism responsible for this epidemic was of a mild strain. The natural immunity possessed by these infants was sufficient to resist and counteract the effects of the gonococcus or its toxin. A singular feature in this connection is the fact that not a single death occurred in the entire group of sixty-seven cases.

As an illustration of the remarkable resistance of only one of these infants, a girl, aged 7 weeks, was admitted to the hospital practically moribund, profoundly toxic and dehydrated. Nine infected joints, mostly of the suppurative type, were discovered. From the knee joints alone, 16 cc. of creamy pus was aspirated. The rectum and vagina were discharging profusely, and a huge ischiorectal abscess was noted. In spite of the profound pyemic process, recovery ensued promptly on incising and draining these suppurating foci. No vaccines were employed in this case.

### SUBACUTE AND CHRONIC STAGES

Extending over a period of three months until the present time, the infants, on their discharge from the hospital, were referred to the outpatient clinics of the Mt. Sinai Hospital for treatment. Those with vaginitis and proctitis were treated in special clinics three times a week. At the end of about one year, most of the infants were cured. Smears were repeatedly negative with few pus cells.

There were thirty-eight infants with joint sequelae who were referred to the physiotherapy clinic, where they were treated by baking, diathermy, massage, etc. Six of the infants with mild complications in the joints were discharged about two and one-half months after the onset of the acute infection. At the end of five months, fifteen children were discharged with restored function of the joints. The other cases were more refractory to treatment.

Foot and wrist drops, contractures of the knee and elbow and pathologic dislocations of the hip joints were the most troublesome of the sequelae. At the end of a year, the pseudopalsies, treated by splints

and electricity, had completely disappeared. It is of interest to note that although an intense inflammatory reaction in the peripheral nerves existed, no permanent changes have intervened. The resistance of nerve tissue to the infection is an interesting observation.

The flexion contractures in the cases showing involvement of the knees and elbows ranged between 10 and 30 degrees. These were due to fibrosis of the flexors and ligaments. In two instances, the head of the tibia was subluxated posteriorly; in one of these cases tenotomies of the hamstrings were found necessary, at 15 months of age, before a cure could be obtained. The other cases responded slowly but progressively to treatment. At the end of eighteen months, normal range of motion was restored. Periarticular hyperplasia, however, still persists, even at the present time, the infants now being 2½ years old. Close inspection shows a slight increase in circumference of these joints. The roentgen ray, however, does not show any bony hypertrophy. These abnormalities are of no significance.

In three cases showing involvement of the shoulder, mild contractures of the scapulohumeral and pectorohumeral muscles seem to persist. These are being treated by passive manipulation and massage.

The treatment of dislocations of the hip was instituted when these children were 18 months of age. Eleven were admitted to the hospital, placed on Bradford frames, and weight extension applied; two weeks later, closed reductions were attempted under ether anesthesia. Considerable difficulty in manipulating these joints was encountered, owing to the fibrosis and contracture of the periarticular tissues. It was impossible to reduce the hip joints in most of the cases at the first attempt. The limb was abducted and flexed so as to bring the femoral head below and posterior to the acetabular cavity. Casts were then applied and maintained for about five weeks. Subsequently, attempts were again made to force the femoral head into the acetabular cavities, in nine of which reduction was accomplished. These were checked up by the roentgen ray.

My associates and I were much elated at the time with such results, but unfortunately, owing to the neglect of the parents and the age of the children, the retentive casts had to be changed frequently because they became soiled or broken. Apparently, it was a case of love's labor lost. All of these dislocations relapsed, largely because of the structural damage to the joints.

Recently, five of these children were readmitted to the hospital and after a month of extension, another attempt was made at reduction. In three, the hip joints were opened through the Smith-Peterson incision. I found the acetabular cavities obliterated, being filled with scar tissue. The femoral heads were above and posterior to the acetabulae, and resembled knoblike protuberances eccentrically situated to the inner side

of the upper end of the femur. After the acetabular cavities were cleaned out as thoroughly as possible, the head of the femur was replaced into the cavity. The operative wounds were closed without drainage; both limbs were fixed in extension abduction and internal rotation, and were maintained in this position by a plaster of Paris spica. There was no postoperative shock. The other two dislocations were reduced by the closed method.

The results of this recent attempt show successful reduction in two of the cases in which operation was performed and in one in which the closed method was used. The other two hips have slipped out. These children are still in casts. Of the six previously treated, new articular facets have formed above the destroyed cavities, apparently of sufficient depth to retain the head of the femur in position.

Relative to the ultimate outcome of the entire group of dislocations of the hip, a favorable prognosis cannot be predicted. Even in the cases in which reduction was successful, the hip joints are abnormal. The damage to this articulation is irreparable.

## CONCLUSIONS

1. Periodic examinations of hospital help and routine bacteriologic studies of cervical and vaginal smears of expectant mothers before admission to maternity hospitals are prophylactic measures in eliminating these as possible sources of gonorrhea.

2. The importance of an early diagnosis of gonococcus sepsis in the new-born housed in hospitals cannot be too strongly emphasized. The disease once introduced into such institutions spreads with incredible rapidity infecting all new-born infants who are exceedingly susceptible to the infection. Such prodromal symptoms as mild elevations of temperature, skin eruptions, superficial abscesses and swelling of the joints should make one suspect the presence of gonorrhea, the diagnosis of which can be made in the early stages by rectal and vaginal smears and bacteriologic studies of joint exudates.

3. The rectum is a portal of entry for gonococci that hitherto has not been sufficiently stressed. The organisms invade the blood stream shortly after the initial local implantation and rapidly metastasize to predisposed joints.

4. Two forms of gonococcus arthritis are observed in infancy—one accompanied by a great deal of swelling and tenderness suggesting suppuration and the other, a subacute synovitis with effusion. Multiple arthritis is the rule in 75 per cent of the cases.

5. Infantile joints, because of their cartilagenous nature, display a marked resistance to the infection. Suppuration of the joints exceedingly damaging to the adult articulations and producing terminal ankyloses was not observed as sequelae in any of the cases.

6. Gonococci may invade the medullary cavities of the long bones and set up localized destructive processes. Spontaneous recovery occurs, as proved by the roentgen ray.

7. The hip joints were the most serious of the complications, becoming spontaneously dislocated in the early stages of the infection. The prognosis in these cases is not favorable, owing to the structural damage to the acetabular cavity and femoral head.

8. Casts, aspirations, incisions and diathermia are the remedies *par excellence* in the treatment of gonorrheal arthritis. Vaccines are of doubtful value.

9. The effect of the gonococcus infection on the epiphyses was to retard their growth, delay the appearance of centers of ossification and in cases of the capital epiphyses of the femur and humerous to produce fragmentation and even complete absorption.

10. The sequelae are best treated by physiotherapy. The dislocations of the hip joints should not be reduced before 2 years of age.

# VOLVULUS

## REPORT OF A CASE IN AN INFANT AGED FIFTEEN DAYS*

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I. D. was born, Dec. 31, 1926, at full term, and weighed 6 pounds 8 ounces (2,954.35 Gm.).

The mother and father were healthy; the mother, a primipara, was 30, and the father, 32. Delivery was spontaneous and normal in every way. Resuscitation was easy.

It was noticed from the time of birth that the infant vomited every time it took water. Vomiting became more marked after the mother's milk appeared (third day). On this day, vomiting was noted to be more definitely projectile in character. Also, visible gastric peristaltic waves were seen. These waves, while definite, were not quite so deep as those seen in congenital hypertrophic pyloric stenosis. Castor oil was given on the third day, and the next day the stool contained a few milk curds for the first time. Before this the feces had consisted entirely of meconium.

On the fourth day, barium was administered by catheter under the fluoroscope. The esophagus was slightly larger than normal. The stomach was of normal size and shape and took 30 cc. of barium mixture easily. Pressure over the stomach by the examiner's hand forced only a small amount of barium into the duodenal cap. No barium could be seen in the pylorus itself for a space of about 1 inch. Roentgen-ray examinations four hours and forty-eight hours later revealed about 50 per cent of barium still in the stomach and a small amount scattered through the intestinal tract.

Atropine sulphate, $\frac{1}{1000}$ grain, by hypodermic every three hours for forty-eight hours ($\frac{1}{40}$ grain [0.0016 Gm.] in twenty-four hours) had no effect on vomiting attacks.

A diagnosis of partial obstruction in the region of the pylorus or duodenum was made. Preoperative diagnoses were: (1) partial atresia of duodenum; (2) duodenal bands; (3) congenital hypertrophic pyloric stenosis.

On Jan. 5, 1927, the sixth day of life, laparotomy was performed. The whole gastro-intestinal tract was examined, special attention being paid to the pylorus and duodenum. No abnormality of any kind was discovered. A stab wound was made in the stomach, and a curved hemostat was passed through the pylorus and duodenum; the blades were then opened and the hemostat was withdrawn. No obstruction of any kind was encountered.

The postoperative diagnosis was pyloric spasm.

The infant continued to vomit after operation as before. During this time the loss of weight was not great (9 ounces [255 Gm.] in six days since birth), showing that a good deal of milk was getting through the obstruction.

There were days when the infant did not vomit so much and days when she seemed to vomit almost everything. The vomitus consisted of yellowish fluid and mucus. The bowels were kept open with milk of magnesia and enemas. Gastric lavage gave inconsistent results.

For two days (the twelfth and thirteenth days of life) the infant was put on a milk formula, and vomiting almost ceased. On the fourteenth day, however, it became restless and was apparently in great pain. Vomiting began again. Several strands of bloody mucus were passed by bowel. The abdomen, which had been flat until now, became distended. Enemas at first brought away feces, and then nothing but blood tinged strands of mucus.

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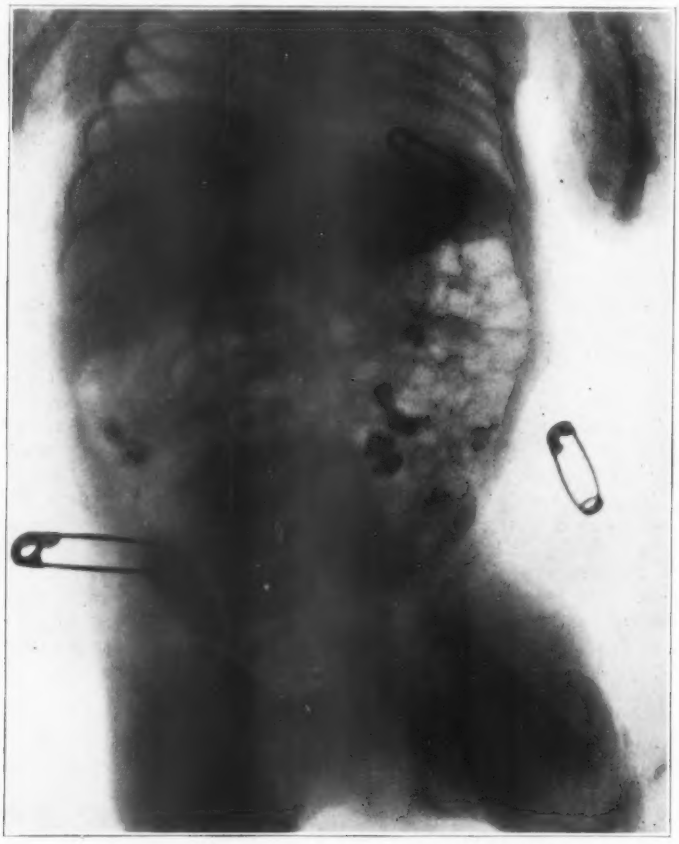
* Received for publication, Feb. 8, 1927.

Diagnosis of intestinal obstruction was made, and laparotomy performed. A segment of gangrenous small intestine containing a perforation and general peritonitis were discovered. A catheter was inserted into the intestine and sutured to the abdominal wall. The infant died two hours after operation.

At autopsy, only the intestinal tract was examined. The stab wound in the stomach made at operation nine days before was almost healed. There was a volvulus of a segment of ileum, which caused complete obstruction. The intestine and mesentery in the twisted segment were gangrenous. Obstruction occurred about one foot above the ileocecal valve.



Roentgenogram taken twenty-four hours after the administration of barium. A large quantity of barium is still in the stomach and a small amount in the intestines.

COMMENT

The interesting question about this case is, What relation, if any, was there between the volvulus and the pyloric spasm? Patients who come to operation with volvulus sometimes give histories of previous similar attacks of abdominal pain and vomiting, which disappear spontaneously.[1] It is plausible to believe that in this case volvulus might

1. Pybus: Surgical Diseases of Children, p. 298.

have been present from birth, and although it could not have been sufficient to cause complete obstruction or even to be noticed at operation, it could have caused sufficient disturbance of intestinal motor function to produce pyloric spasm. It is believed by some that pyloric spasm is always secondary to some other disturbance.[2]

2. Richter, in Abt's Pediatrics, vol. 3, p. 476.

# PROGRESS IN PEDIATRICS

## UROLOGIC PROBLEMS IN INFANCY AND CHILDHOOD*

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At the present time, there is a general appreciation of the importance of subjecting to a complete urologic survey every patient who presents symptoms and signs pointing toward lesions of the genito-urinary tract. Unfortunately, the same feeling of responsibility and the same point of view are not at hand in the case of an infant or a child. Yet it is a well recognized fact that during infancy and childhood practically all of the various lesions of the urinary tract that are encountered in adults present themselves for diagnosis and treatment. There are two exceptions to this statement: enlargement of the prostate does not occur, and carcinoma is exceedingly rare. Formerly many adults were treated by means of internal medication without any attempt to determine the cause of the disorder, and were carried along beyond any reasonable time during which a cure might be expected. Today the same relative situation exists in the domain of infancy and childhood.

There are many factors that might explain in part this state of medical procrastination. Perhaps it is not generally recognized that complete urologic study is possible in infancy and childhood. It is only in recent times that the textbooks on pediatrics give any space to the instruments of precision that can be used in this field. Failure to acquaint medical students in the past with this possibility was due, in a certain measure, to the fact that this knowledge was not widespread. Pediatricians often hesitate to avail themselves of these modern methods of diagnosis that are available, and many of the little patients are treated medically or expectantly with the hope that the condition will clear up. The result is that a serious organic disease thus treated often causes irreparable injury to vital organs, which might have been prevented by an early recognition and removal of the cause.

### AGE

In the early period of prostatic surgery, there were many who objected to subjecting elderly men to cystoscopic examination and operation because of the fact that they were of advanced age. A reverse

* Read by invitation at the Annual Meeting of the Philadelphia Urological Society, Jan. 24, 1927.

situation greets one in dealing with infants and children. Because they are so young and so small, it is suggested that they should not be subjected to cystoscopy, ureteral catheterization, etc. The same situation exists in other departments of medicine as well. I am told by my neurologic colleagues that the same alibi is used when the question of lumbar puncture in children comes up. It is a well-known fact that children stand instrumental examination well, and it is the general concensus among urologists who have done much urologic study of infants and children that not only do children stand instrumental examination well but the reaction is less than in adults. It is not so many years ago that cases in which cystoscopy and ureteral catheterization had been carried out in infants and young children were reported because of the extreme rarity of instrumental examination.

In a review of this series of cases, it will be found that there are seven children who were under 12 months of age. The youngest child

TABLE 1.—*Ages*

| | No. Cases | | No. Cases | | No. Cases |
|---|---|---|---|---|---|
| 27 days | 1 | 2 years | 5 | 8½ years | 1 |
| 5 weeks | 1 | 2½ years | 3 | 9 years | 2 |
| 5 months | 1 | 3 years | 6 | 10 years | 6 |
| 7 months | 1 | 3½ years | 1 | 11 years | 3 |
| 8 months | 1 | 4 years | 6 | 12 years | 5 |
| 11 months | 2 | 5 years | 5 | 13 years | 5 |
| 13 months | 3 | 6 years | 6 | 14 years | 5 |
| 18 months | 1 | 7 years | 5 | Not stated | 4 |
| 20 months | 1 | 8 years | 6 | | |
| Total | | | | | 86 |

on whom a cystoscopic examination was made was a boy, 27 days old. The youngest boy in whom the ureters were catheterized and pyelograms made was 5 months of age. The youngest girl in whom the ureters were catheterized and pyelograms made was 7 months of age. Naturally a larger number of cystoscopies were performed and ureters catheterized in the older children. A reviewing of this series of cases, as well as a review of the case reports in the literature, leads to only one conclusion, namely, that age can no longer be used as an alibi and an argument against careful, complete urologic survey in infancy and childhood.

Deming [1] has made a cystoscopic examination, catheterized the ureters and made pyelograms of an infant, aged 29 days. Seaman [2] has reported an infant, aged 4 months, in whom cystoscopy had been performed and the ureters catheterized.

1. Deming, C. L.: Congenital Sarcoma of Kidney in Child of Twenty-Nine Days, J. A. M. A. **80**:902 (March) 1923.

2. Seaman: Boston M. & S. J. **195**:623 (Sept. 23) 1926.

SEX

In this series of cases there are thirty-four boys and fifty-two girls.

It does not seem as though sex made much difference in this series, in regard to urologic lesions, except the fact that pyelitis occurred more frequently in infant girls than in boys. Pyelitis was found in twenty-five girls and in two boys. It can be said without reservation that cystoscopy and ureteral catheterization can be carried out much more easily in girls than in boys, it being necessary only to dilate the short urethra in the former, whereas in the latter an external urethrotomy has been advocated by some authorities. In regard to this procedure, my experience has taught me that its performance is not necessary.

ONSET

A careful survey of the cases in this series was made with the object of determining the time that elapsed between the onset of the illness and the time when the patients presented themselves for investigation.

TABLE 2.—*Cases According to Age*

| | No. Cases | | No. Cases | | No. Cases |
|---|---|---|---|---|---|
| 5 days | 1 | 4 months | 2 | 2½ years | 4 |
| 7 days | 1 | 5 months | 2 | 3 years | 5 |
| 8 days | 1 | 7 months | 5 | 4 years | 4 |
| 2 weeks | 2 | 8 months | 2 | 5 years | 2 |
| 3 weeks | 2 | 12 months | 7 | 5½ years | 1 |
| 4 weeks | 4 | 14 months | 2 | 6 years | 1 |
| 6 weeks | 3 | 18 months | 2 | 8 years | 1 |
| 2 months | 3 | 20 months | 1 | 12 years | 2 |
| 3 months | 1 | 22 months | 1 | 14 years | 1 |
| 3½ months | 1 | 2 years | 4 | Not stated | 18 |

Table 2 shows the period of time that elapsed between the onset of the symptoms and the cystoscopic examination. There may be a slight discrepancy in some of the figures; for example, the patient may have been suffering from a particular ailment for a long time before a physician's services were engaged. It stands to reason that when this occurs the interval between the time the symptoms appeared and the examination would be relatively short, and necessarily would not be a true index of the duration of the trouble. As an illustration, in a case in which there has been a sudden block of the ureter and subsequent hydronephrosis, the onset of the hydronephrosis might be thought the beginning of the trouble, which is a wrong calculation, since for a long time treatment may have been given for another condition, such as pyelitis.

One obtains the impression (from the histories in this series) that these patients are often carried along on medical treatment for exceedingly long periods without justification. Far be it from me to state that every child with pus in the urine or urinary symptoms should be rushed into a cystoscopic examination. On the contrary, it is my firm belief that such a procedure would be decidedly wrong, and that these patients

should be given the benefit of medical treatment, especially in cases of infection in the urinary tract or so-called cases of acute pyelitis. The patients should have rest in bed with the administration of large quantities of fluid, as much as 2,500 or 3,000 cc. in twenty-four hours. The use of alkalis or alkaline diuretics can be carried out, and this can be alternated with administrations of acid phosphate of soda and methenamine. But if the pyuria persists in spite of a careful regimen for its cure, then the reason for the persistence of the pyuria should be determined, which amounts to saying that one ought to determine the underlying pathologic change.

### OBJECTIONS TO CYSTOSCOPY IN CHILDREN

Whenever the subject of cystoscopy and ureteral catheterization is mentioned as the next procedure in order in any given case, objections naturally arise, and it may not be amiss to dwell on some of the more frequently mentioned objections as I have encountered them.

1. *Major Procedure.*—Probably the most frequently voiced objection is that cystoscopy and ureteral catheterization in children constitute a major undertaking, and for this reason firm objection is raised. Exactly the same objection was raised twenty years ago whenever cystoscopy and ureteral catheterization were mentioned as the best procedure in adults. That this is not a major procedure must be evident to those who have had occasion to work with urologists or to those who have had patients examined; hence, I am sure that urologists will be convinced that these objections are not well founded. Naturally, the more frequently these examinations are carried out, the more skilful and dexterous the operator becomes. Efficiency counts for a great deal in making cystoscopy and ureteral catheterization simple procedures, whereas inefficiency results in keeping both in the class of major procedures. Again, the objection is sometimes voiced not because cystoscopy and ureteral catheterization are looked on as major procedures, but by way of a defensive reaction, since cystoscopy in children was rather uncommon and a relatively new form of examination until recently.

2. *Use of an Anesthetic.*—That many of these little patients require an anesthetic goes without saying. The anesthesia is of only a few minutes' duration, as it rarely, if ever, requires more than three or four minutes to examine the bladder and to catheterize the ureters. Whenever possible, ethylene anesthesia should be used. In my opinion no objection should be raised against a five minute examination under this form of anesthesia, since the outcome is much valuable information toward clearing up a doubtful or obscure problem. Even when the administration of ether is necessary, the anesthesia is of such short

duration that objections are out of order. Mention should be made here of the decreasing number of patients who require general anesthesia and the increasing number on whom cystoscopy and ureteral catheterization can be done under local anesthesia without causing suffering.

Fig. 1.—Pyelogram made to exclude hydronephrosis in a boy, aged 5 months.

3. *Danger.*—It goes without saying that any sort of instrumental examination is not entirely devoid of danger, particularly if one bears in mind the fact that many of these patients who require instrumentation harbor infectious elements in the urinary tract and that injury might result which may permit the spread of organisms into the circulation unless great care is exercised in the passage of instruments. It should be added that injury is of rare occurrence.

4. *Severe Reaction.*—Severe reaction following cystoscopic examination was extremely rare in this series of cases. This possible objection has been mentioned several times and is based, I believe, on the experiences practitioners have had with their adult patients. It is a well-known fact that there are a certain number of patients who tolerate poorly any sort of instrumental examination; cystoscopy and ureteral catheterization are not exceptions to this rule. My experience, however, does not substantiate these statements; rather, the reverse is the case. It has been my experience that these little patients show less reaction after cystoscopy, ureteral catheterization and pyelograms than adults do, and, moreover, that they stand urologic examination well. Recently, Lowsley and Butterfield [3] have reported similar experiences.

## INDICATIONS FOR CYSTOSCOPY

The indications for cystoscopic examination are exactly the same in infancy and childhood as in adults. The verification of these indications may at times be difficult, since many children cannot accurately describe their symptoms. Especially is this true in the treatment of infants, when one must rely on the statements of the mother or nursemaid, whose powers of observation may not be keen.

The symptoms that most frequently bring the little patients in for examination are: (1) the presence of pus in the urine with or without recurring attacks of pyelitis; (2) the presence of blood in the urine; (3) the presence of tumors in the abdomen; (4) the presence of various urinary symptoms, and (5) for the exclusion of lesions of the urinary organs. Because of the age of some of these patients, certain symptoms and signs may not be mentioned by the mother, the nursemaid or the nurse in the hospital; but it seems to me that in every case a careful history of the patient and a complete physical examination plus a urinary examination will yield a clue that the urinary tract is the source of the condition. A review of these eighty-six cases shows that the following were the reasons most frequently found for having the patient subjected to cystoscopic examination and ureteral catheterization.

1. *The Presence of Pus in the Urine With or Without Recurring Attacks of Pyelitis.*—Pus in the urine was the most frequent single indication for urologic examination, having been found in sixty-six cases. The presence of pus was part of either a recent or a remote attack of pyelitis. The majority of the patients had had one or more attacks of pyelitis before coming under observation, but a few of them were seen during an acute attack. The fact that pus in the urine did not respond to the usual forms of treatment was one of the common reasons for cystoscopic study. In another group belong the cases of persistent pyuria but without any recent or remote manifestation of acute pyelitis. This is a far smaller, but none the less important, group.

3. Lowsley and Butterfield: J. Urol. **16**:415 (Dec.) 1916.

2. *Presence of Blood in the Urine.*—Whether blood in the urine occurs in infancy and childhood or in adults, it is always significant of organic disease in the urinary tract. In this series, thirty-two patients had blood in the urine, and in several instances complaint was made of

Fig. 2.—Hydronephrosis in a girl, aged 12 years. This figure should be compared with figure 3.

profuse bleeding. I should like to emphasize here that every patient having profuse bleeding in the urinary tract, unless it is caused by an acute nephritis, should be subjected to urologic study.

3. *Abdominal Tumor.*—The presence of tumors in the abdomen is often discovered by accident by the parent, without any history of

symptoms. These tumors demand investigation. In this series they were of two types. The first is caused by malignant disease of the kidney. Pyelograms, as a rule, are not made as often in infancy and childhood as they are in adults; nevertheless, there are cases in which a pyelogram should be made, otherwise the clinical diagnosis of renal malignancy cannot be verified. The second type is hydronephrotic tumors. There were a number of patients who came in with symptomless abdominal tumors, the origin of which was not clear. In these instances, urologic study at once was made to determine the origin and nature of the tumor. Some of the mothers ventured a statement that the tumor was not always of the same size and that at times it appeared smaller. In each instance in which this statement was made, a hydronephrosis was found. In one case of recent date, in which the tumor was in the left upper quadrant, the problem called for a differentiation between spleen and kidney.

4. *Urinary Symptoms.*—In the main, the urinary symptoms in children correspond closely to the symptoms that would be present in a similar series of cases in the adult, with the exception that hematuria would probably be more frequent in the adult. Urinary symptoms of one sort or another often bring these patients in for study. A further discussion of the symptoms noted in this series will be mentioned further on in this paper.

5. *To Exclude Lesions of the Urinary Tract.*—Most of the publications which deal with this topic and in which a large series of cases were reported dealt for the most part with positive symptoms. Urology, until recently, has been concerned chiefly with establishing, strictly speaking, urologic diagnosis.

Lately, however, the urologist is called on more and more to institute differential abdominal diagnoses and frequently to differentiate between lesions of the right upper quadrant and the right kidney. As this special field becomes developed more and more and as the pediatricians avail themselves of this help, the variety of cases will become more and more varied and interesting, so that the urologist will find more cases in which his observations are negative. In this series there are five cases in which consultation was decided on in order to rule out organic disease of the genito-urinary tract, not negative observations. Because of certain urinary symptoms, the patients were put through the usual routine urologic examination, with negative observations. The value of this procedure in doubtful and borderline cases can hardly be questioned.

## METHOD OF PROCEDURE

The entire subject of urology in pediatrics does not differ from urology in adults, except that in dealing with infants and children one must, of necessity, work with smaller instruments. Another impor-

tant point is to remember that those who are engaged in this field of work must develop their technic so that they can handle the small instruments with precision. I have made it a rule to carry the little patients through a definite routine, performing cystoscopy and ureteral catheterization last and not first. In order to standardize this method of examination, the following routine has been developed:

Fig. 3.—Pyelogram showing normal condition on left side. This figure should be compared with figure 2.

1. *History.*—In every instance, as complete and careful a history as is possible is obtained. A good many times important points are elicited in the histories, and in case all the information desirable cannot be obtained from the mother the first time the patient is seen, a supplementary history two or three days later or on succeeding days is elicited.

This is an important point, because so many times a complete history gives one a direct clue in regard to the patient's underlying condition. It is not at all unusual to elicit a history of some acute antecedent infection before the onset of the symptoms of pyelitis. Gastro-intestinal upsets and tonsillitis seem to be the precursors most frequently mentioned. Not at all uncommon is the statement that these patients have had a cold in the head or influenza. In several instances, the first symptoms were noted after an attack of measles.

2. *Physical Examination.*—A complete physical examination is the next step in order, and the patients should be given the benefit of a careful, complete physical examination, just as is done in adults. Needless to say, this should include a careful search for foci of infection. I cannot say with certainty that these foci play a rôle in the causation of infection in the urinary tract in infants and children, but whether or not this is the case, the search for foci should not be carried out at the expense of other methods of examination. For example, in the desire to determine their presence, one should not forget to make careful and often repeated examinations of the urine. A complete physical examination often reveals many things that are direct aids in establishing a diagnosis.

TABLE 3.—*Elements Found in Urine*

| | No. Cases | | No. Cases | | No. Cases |
|---|---|---|---|---|---|
| Pus | 67 | Blood | 32 | Sugar | 2 |
| Albumin | 37 | Casts | 16 | Not stated | 7 |

3. *Urinary Analysis.*—The third step to be carried out is the careful examination of the urine. If the patient happens to be a boy, it is simple and easy to obtain a sterile specimen. In the male, the specimens are obtained by cleaning the penis with soap and water and bichloride, inserting the penis in a sterile test tube and holding this in place with adhesive. In girls, under aseptic precautions, a soft rubber catheter is introduced into the bladder and a sterile specimen is obtained. Examination of the urine thus obtained yields considerable information. Pus, red blood cells and bacteria are the three elements most frequently found. Of course, as time goes on and as cystoscopies are done and the ureters catheterized, more detailed studies of the urine are undertaken. Often a specimen obtained on admission shows the presence of pus and bacteria, and because of this attention is immediately focused on the urinary tract as the source of the illness. Of all measures at one's disposal, examination of the urine yields the greatest amount of information that can be obtained without much effort; yet one often is called in consultation to see a patient whose urine has not been analyzed. Table 3 is illustrative of what is found on urinalysis.

4. *Roentgen-Ray Examination.*—The next step pursued is the roentgen-ray examination of the urinary tract. This is carried out with the object of demonstrating stones at any point in the urinary tract if they should be present. Besides stones, the examination may show the

Fig. 4.—Right hydronephrosis and hydro-ureter due to a stricture at the ureterovesical junction. This figure should be compared with figure 5.

presence of calcification, when tuberculosis of the kidney is suspected. It is generally believed that the calcification in renal tuberculosis is rare in infancy and childhood; however, such is not my experience, since calcification was present in three of the five cases in this series.

5. *Examination for Residual Urine.*—This is a simple thing to do; it can be carried out without an anesthetic and often gives the most valuable information. In small children, the examination ought to be repeated several times so as to be sure of what is found. The largest amount of residual urine found in this series was 285 cc. At the close of this examination, one then proceeds to the next step:

6. *Cystography.*—Cystography is not done as a routine, because in the average case it is not indicated. There are certain times when this relatively simple procedure should be carried out, as it yields valuable information before the cystoscope is used. In cases in which the physical examination shows a suprapubic tumor, a cystogram, after the residual urine is estimated, will show the size, form and position of the bladder together with the presence of diverticula, their size, location and number. In a certain group of cases ureteral reflux is shown not only in a most graphic manner, but also when least expected. This phenomenon has been seen in three groups of cases: (*a*) In cases showing pathologic change at the ureteral orifice, in which that orifice is open, the solution put into the bladder finds its way into the kidney pelvis; (*b*) cases in which the ureteral openings are normal may show a reflux up the ureter (Kretschmer[4]); (*c*) reflux from the bladder up the ureter into the kidney pelvis has been seen during the course of ureteral catheterization at various times in cases in which the ureteral orifice, as seen with the cystoscope, was normal. This phenomenon was reported many years ago by Hagner of Washington.

7. *Tests of Kidney Function.*—Next in order is a study of the renal function. This can be carried out by measuring the fluid intake and the fluid output, estimating the specific gravity of urine and making a test of the output of urea. Examination of the chemistry of the blood should be carried out in every case before cystoscopic examination is undertaken. One occasionally encounters cases in which there is present an enormous dilatation of the kidney pelves and ureters with resulting atrophy of the kidney; these patients are skating on thin ice. If they have just recently weathered the storm of an acute renal infection, a cystoscopic examination and the making of pyelograms may be more of a load than the patients can stand under the circumstances. It would be well always to make it a rule to study carefully the kidney function in the patients before subjecting them to cystoscopy and pyelograms. Mixed thalein tests also can be carried out; some urologists prefer to use indigo carmine.

8. *Cystoscopy, Ureteral Catheterization and Pyelography.*—The last steps in the examination are cystoscopy, ureteral catheterization and pyelography. As far as I know, the first one to perform cystoscopy and catheterization successfully in children was Max Nitze, who made a cystoscopic examination in a boy as young as 8 years of age. Nitze described this case in his "Textbook," in 1907. The following year

4. Kretschmer, H. L.: Surg. Gynec. Obst. **23**:391 (Dec.) 1916.

Portner reported several cases in which cystoscopy and ureteral catheterization were carried out. Among the early workers in this interesting field, in this country, were Beer, Hyman, Hinman, Stevens, Thomas and Tanner. Since 1922, there has been a decided interest in this sub-

Fig. 5.—Left hydronephrosis and hydro-ureter due to stricture at the ureterovesical junction.

ject, and many cases are reported in which this procedure has been carried out. The more that pyelography is employed, the greater are the surprises, because often extensive pathologic changes are demonstrated that were not suspected. It is strange, then, that with this aid at their command, physicians are resorting more and more to the making of

pyelograms? In my opinion it is not necessary to make routine pyelograms in each case, but, on the other hand, when a diagnosis cannot be made without resorting to the use of the pyelogram, there should be no hesitation whatever in employing this useful diagnostic aid. Pyelography should be carried out at the time that the first ureteral catheterization is done if there is any doubt of the underlying pathologic change. If, for example, one decided to carry out pelvic lavage because of an infection from *B. coli,* it is a better plan to make pyelograms first instead of subjecting the patients to a course of unnecessary pelvic lavage only to find that the procedure is not giving the patient the desired relief, and to discover, after the pyelograms are made, a large hydronephrosis or a lesion that may require radical surgery for a cure.

Not only is pyelography of value in showing unsuspected hydronephrosis, strictures of the ureter, etc., but, as is the case with adults, in the small patients, pyelography is employed as the best aid in the differential diagnosis of abdominal tumors. Furthermore, in certain cases pyelograms are made to exclude the presence of organic disease in the upper urinary tract, and also to differentiate cases with or without stasis in the renal pelvis.

Since some of the patients are catheterized under anesthesia, they are allowed to wake up before pyelograms are made. Always being guarded in my selection of cases, it has been my experience that it is surprising how rare are the reactions that are so frequently encountered in adults.

## SYMPTOMS

It has been interesting in reviewing the histories in this series to analyze the symptoms of which complaint was made on admission to the hospital. The elicitation of the symptoms may not always be accurate, because at times a history of the symptoms is compiled from the statements of the mother or nursemaid or a nurse in the hospital or orphanage, who may not be keen in the matter of observation; hence, it is generally assumed that these histories are not accurate. Bearing this possibility in mind when writing the histories of some of the subsequent cases in the series, I paid particular attention to eliciting as careful a history as it was possible to get, under the circumstances. The symptoms, in the main, tally closely with those encountered in the adult, except for the frequency of retention of urine, and this, as one might well imagine, is probably the result of the fact that little children do not have prostatic obstruction. On the other hand, residual urine was always found in the cases of contracture of the internal urethral orifice. A careful review of the histories shows the symptoms given in table 4.

In some of the cases there were no symptoms at all, and the patients were brought in merely because of the accidental finding of a large tumor.

The publications in which large series have been reported have for the most part dealt with positive observations. A review of this series shows that there are five cases in which there were negative observations. In other words, these patients were subjected to urologic survey in order to exclude the presence of pathologic change in the bladder or

Fig. 6.—Bilateral hydronephrosis and hydro-ureter due to a stricture at the ureterovesical junction.

upper urinary tract. In a recent publication of Lowsley and Butterfield,[3] they likewise report a series of cases in which the patients evidently had been subjected to urologic study in order to rule out disease. This, I believe, is another new angle in the study of urology and pediatrics that is attracting attention and is a logical procedure in doubtful and bor-

derline cases. Since the early periods, urology has dealt too strictly with urologic lesions, and the fact that differential diagnosis is at least as important as the problem of determining whether a patient has a right or a left renal lesion has been overlooked. Lately, however, the field of urology is widening, and, as has already been indicated, the urologist is called on more and more to make a positive differential abdominal diag-

TABLE 4.—*Symptoms*

| | No. Cases | | No. Cases | | No. Cases |
|---|---|---|---|---|---|
| Fever | 44 | Headaches | 12 | Dribbling | 6 |
| Pain | 35 | Constipation | 11 | Urgency | 5 |
| Cloudy urine | 32 | Diarrhea | 9 | Sand | 4 |
| Frequency | 30 | Burning on urination | 8 | Backache | 2 |
| Hematuria | 26 | Difficulty | 7 | Sweats | 2 |
| Vomiting | 23 | Irritability | 7 | Tenesmus | 2 |
| Incontinence | 17 | Nausea | 7 | Retention | 2 |
| Painful urination | 16 | | | | |

TABLE 5.—*Lesions Found at Operation*

| | No. Cases | | No. Cases |
|---|---|---|---|
| **LESIONS OF THE KIDNEY** | | | |
| Pyelitis | 27 | Chronic pyelonephritis | 3 |
| Tuberculosis | 5 | Chronic nephritis | 2 |
| Sarcoma | 3 | Acute nephritis | 1 |
| Hemorrhagic nephritis | 3 | Stone | 1 |
| **LESIONS OF THE BLADDER** | | | |
| Stone | 4 | Angioma | 1 |
| Contracture of bladder neck and diverticula | 3 | Gonorrheal cystitis | 1 |
| | | Trigonitis | 1 |
| **LESIONS OF THE URETER** | | | |
| Stricture with hydronephrosis | 10 | Prolapse | 1 |
| Stone | 2 | | |
| **LESION OF THE URETHRA** | | | |
| Congenital valves in posterior urethra | 1 | | |
| **LESIONS OF THE NERVOUS SYSTEM** | | | |
| Spina bifida | 3 | | |
| **MISCELLANEOUS LESIONS** | | | |
| No pathologic change found, examination negative | 5 | | |
| Appendicitis | 2 | | |
| No diagnosis made | 7 | | |

nosis. In obstinate cases in adults it is his métier to rule out the presence of disease in the upper urinary tract, and it is not hard to visualize a similar situation in the field of pediatric urology. In five of this series of cases consultation was decided on in order that organic disease of the urinary tract might be ruled out, and in one case a cystoscopic examination was done in a boy, aged 5 weeks, to rule out a lesion of the bladder—at operation a large appendical abscess was found. The various lesions found are presented in table 5.

THE LITERATURE

Proof of the gradual growth of the interest in the urologic problems in infancy and childhood is shown in the increasing number of papers that are being published on the subject. Probably the first paper published in this country was that of Beer,[5] in March, 1911, on "Cystoscopy and Ureteral Catheterization in Young Children." At

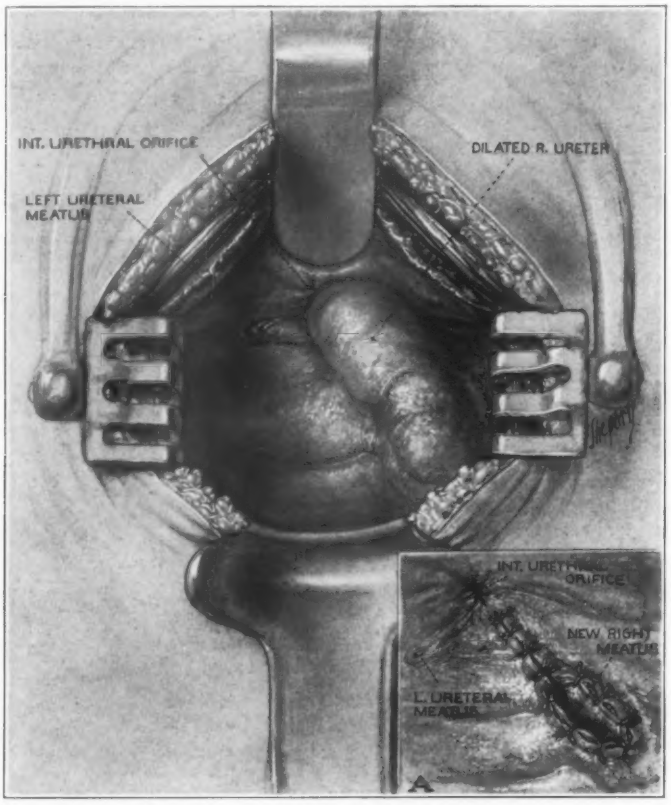


Fig. 7.—Prolapsed dilated right ureter which impinged on the internal urethral orifice. Insert *A* shows the new right ureteral orifice.

rare intervals articles were published by O'Neil[6] on "Bladder Tumors in the Young," by Hyman[7] on "Surgical Diseases of the Urinary Tract in Children," and by Hinman[8] on "Results of Cystoscopic

5. Beer: Am. J. Surg., March, 1911.
6. O'Neil: Boston M. & S. J. **173**:873 (Dec.) 1915.
7. Hyman, A.: Urinary Tract Surgery, Am. J. Dis. Child. **15**:116 (Feb.) 1918.
8. Hinman, F.: Cystoscopic Study of Urologic Conditions in Children, Am. J. Dis. Child. **17**:305 (May) 1919.

Studies in Children." Kretschmer and Helmholz [9] have reported a series of "Cases of Pyelitis that were Treated by Pelvic Lavage." Quinby [10] recorded his experience with pyelitis in children, and Eisendrath [11] reported a series of cases of stricture of the ureter.

Since 1920, the publications on this subject have appeared more frequently. In 1924, many urologic topics were considered from various angles by Wright,[12] Smith,[13] Beer,[14] Deming,[1] Hinman and Kutzman,[15] Craig,[16] Bugbee and Wollstein,[17] and in 1926 papers were published by Patch,[18] Pugh,[19] Graham,[20] Hyman,[21] Bugbee,[22] Mixter,[23] Stevens,[24] Caulk,[25] Grant [26] and McKay.[27] Other articles are by Frontz,[28] Hinman,[15] Hyman,[29] Kretschmer,[30] Beer [31] and Deming.[32]

The natural inference is that as time goes on and the interest in this subject becomes awakened, more and more of the little patients will be subjected to careful investigation; many interesting cases will be found and reported, with a steadily growing literature on the subject. As one reviews the literature, one is impressed with the difference between the character of the recent publications, based, as they are, on detailed urologic study, and that of the older publications, which dealt only with more obvious lesions—those easily recognized without the assistance of special aids; for example, such subjects as pyelitis, tumors of the kidney, extrophy of the bladder and vesical calculus.

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9. Kretschmer, H. L., and Helmholz, H. F.: Treatment of Pyelitis in Infancy and Childhood, J. A. M. A. **75**:1303 (Nov.) 1920.
10. Quinby, W. C.: Pyelitis in Children, J. A. M. A. **68**:591 (Feb.) 1917.
11. Eisendrath: Ann. Surg. **65**:552 (May) 1917.
12. Wright, B. W.: California and West. Med. **22**:313 (July) 1924.
13. Smith, C. K.: J. Oklahoma M. A. **17**:242 (Oct.) 1924.
14. Beer: Internat. Clin. **3**:272 (April) 1923.
15. Hinman, F., and Kutzman, A. A.: Ann. Surg. **80**:569 (Oct.) 1924.
16. Craig: Supp. to M. J. Australia, March, 1924, p. 91.
17. Bugbee, H. G., and Wollstein, M.: Surgical Pathology of Urinary Tract in Infants, J. A. M. A. **83**:1887 (Dec.) 1924.
18. Patch, F. S.: Canad. M. A. J. **15**:8 (Jan.) 1925.
19. Pugh: Urol. & Cutan. Rev. **24**, no. 7, 1925.
20. Graham: Am. J. M. Sc. **170**:401 (Sept.) 1925.
21. Hyman, A.: J. Urol. **9**:431 (May) 1923.
22. Bugbee, H. G.: New York State J. Med. **25**:1063 (Dec.) 1925.
23. Mixter, C. G.: Ann. Surg. **84**:533 (Oct.) 1926.
24. Stevens, W. E.: Diagnosis and Treatment in Pathologic Conditions of Urinary Tract in Children, J. A. M. A. **77**:1081 (Oct.) 1921; California and West. Med. **23**:294 (March) 1925; **24**:57 (Jan.) 1926.
25. Caulk: Southern M. J. **19**:351 (May) 1926.
26. Grant, O.: J. Urol. **16**:137 (Aug.) 1926.
27. McKay: Southern M. J. **19**:460 (June) 1926.
28. Frontz: Southern M. J. **15**:570 (July) 1922.
29. Hyman: Surg. Gynec. Obst. **41**:298 (Sept.) 1925.
30. Kretschmer, H. L.: Footnote 4. Urologic Surgery in Pediatrics, J. A. M. A. **79**:286 (July) 1922.
31. Beer, E.: Ann. Surg. **79**:264 (Feb.) 1924.
32. Deming, C. L.: Surg. Gynec. Obst. **39**:432 (Oct.) 1924.

Thus, in a review of papers from the recent literature, made rather at random, there may be found fifty-seven papers dealing with one phase or another of nephritis, thirty-eight on infections of the urinary tract and pyelitis, twelve on pyuria and ten on enuresis. The largest number in this group—seventy-three—dealt with congenital anomalies. There were twenty-three papers on tumors, eleven on polycystic kidneys and several on both urinary and genital tuberculosis. There were seven papers dealing with kidney function tests. Among the other papers one finds a discussion of uric acid infarcts, the elimination of organic acids in the urine, changes in ferments in the urine, malakaplakia, cystinuria, etc.

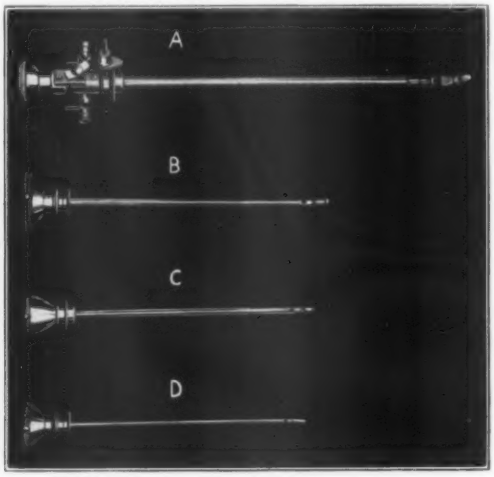


Fig. 8.—*A*, Brown Buerger cystoscope concave with examining lens system; caliber 24 French scale; *B*, Nitze-Ringleb cystoscope for examining children, with Zeiss lens, 12 French scale, upright image, 15 cm. long; *C*, Nitze-Hirshman cystoscope for examining children, caliber 12 French scale, inverted image, 14 cm. long; *D*, Nitze-Wolf cystoscope for examining infants, with Zeiss lens, caliber no. 7 French scale; *B*. Nitze-Ringleb cystoscope for examining children.

## INSTRUMENTATION

A great deal of the credit for the possibility of subjecting these patients to urologic examination is due to the ceaseless ambition and the untiring energy of the various instrument makers through whose efforts the present small but wonderful instruments have been perfected, for without these aids exploration would be limited to the larger children. Strange as it may seem, it is nevertheless true that the profession all over the world is still unfamiliar with the fact that these small instruments have been perfected and may be acquired without any trouble. Bruning,[33] in a recent paper, stated that since cystoscopy is nearly

33. Bruning: Arch. f. klin. Chir. **142**:135 (Oct.) 1926.

impossible in so young a child (his patient was 3 months of age), a diagnosis must depend chiefly on palpation. He quotes three other patients from the literature, one 3, one 5, and one 8 months of age, in whom the diagnoses were limited to the same method. The youngest child examined in this series was a boy, 27 days old, in whom a plain cystoscopic examination was carried out.

### PYELITIS

Of the various lesions of the urinary tract in infancy and childhood, none occurs so frequently as acute and chronic pyelitis, and none has been the subject of so many papers, the burden of the papers being the treatment.

The fact that the treatment is still a matter of so much discussion is strong evidence that there remains a great deal to be desired in regard to treatment.[34] Of course, the fact is recognized by all physicians that many cases run a short course and the patients get well without any treatment.

The second group, which is the largest, represents those cases in which the diagnosis is made, the patients are put on the generally accepted forms of treatment, and in due time they recover. This group, of course, offers no problems in treatment.

The third group, however, is the one great problem and is the large group in which the patients are victims of the ever-recurring attacks or relapses of acute pyelitis. This group also includes the cases of persistent pyuria without febrile manifestations. The problem in this group concerns itself chiefly and mainly with a determination to ascertain the reason for the persistence of pus and colon bacilli in the urine. Aside from the fact that one may assume that the general physical examination is negative, the attention should be directed at once to a complete examination of the urinary tract. As a rule, these patients all have been examined for foci of infection (tonsils and sinuses), and their gastro-intestinal tracts have been put in order. They have had all sorts of alkalis, vaccines, etc., and still the pyuria persists. Who can deny that an examination of the genito-urinary tract is a justifiable procedure if all the usual methods of treatment fail? Many times definite organic disease has been found to be the real reason for the persistence of the pyuria—stones, stricture of the ureter, hydronephrosis and renal tuberculosis. The previously mentioned cases likewise are readily amenable to treatment. With the latter group the question of treatment is not uniform. It is in this group that I [9] have resorted to the use of pelvic lavage with silver nitrate. This therapeutic agent has been a valuable adjunct in the treatment in that it has cleared up many of these cases after all other measures have failed. This has

34. Kretschmer, H. L.: Surg. Gynec. Obst. **33**:632 (Dec.) 1921.

also been the experience of Gordon Craig,[16] who was able to report the results of pelvic lavage in thirteen cases: nine patients were cured, one was relieved, two were unrelieved and one died. The last case should not be included, as it was an infection superimposed on a congenital bilateral intermittent obstructive lesion in the ureters. Although it must be recorded that a small group of cases remains, in which lavage with silver nitrate has failed to render the urine sterile and free of pus, there is no doubt of the fact that it has cleared up a large number of cases after all other forms of treatment had failed.

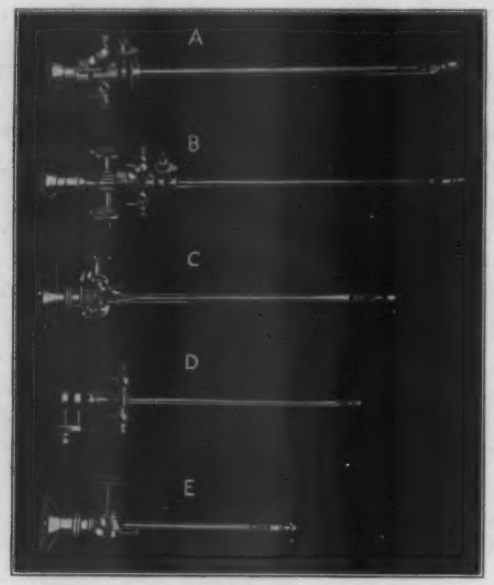


Fig. 9.—*A*, Brown Buerger cystoscope concave with examining lens system; caliber 24 French scale; *B*, Brown Buerger catheterizing cystoscope, caliber 18 French scale; *C*, Nitze-Ringleb double catheterizing cystoscope for children, caliber 17 French scale, 18 cm. long, upright image; *D*, Butterfield's catheterizing cystoscope for infants, caliber 16 French scale, 14 cm. long; *E*, Nitze-Ringleb catheterizing cystoscope for children, single, caliber 16 French scale, extra short model, 13.5 cm. long.

It seems to be reasonable to state that in every case of pyuria in infancy and childhood that does not clear up on medical treatment a complete urologic survey should be made. To carry these patients along for years only to find a seriously injured organ that demands surgical removal is a wilful wrong to them.

Of extreme interest are the cases of pyelitis that occur immediately after birth, the so-called neonatal pyelitis. According to Sauer: (1) the disease occurs periodically and may easily be overlooked; (2) the early symptoms are invariably referable to the gastro-intestinal

tract or the central nervous system; (3) its preponderance at such an early age in male infants may shed some light on the route of infection. Thirteen of Sauer's fifteen patients were boys.

Of further interest may be mentioned six cases of pyelitis in the new-born, recently reported by Dr. R. H. Graham.[20] In his series there are three boys and three girls. He believes that the time of onset in his series suggests an invasion by the bacteria at the time of birth in most cases. His series is interesting.

### STRICTURE OF THE URETER

In this series there are ten cases, three of which occurred in boys and seven in girls.

As time goes on and the literature on this interesting topic grows, it becomes more and more evident that infants and children in the main are subject to exactly the same pathologic processes as are adults, with the exception of malignant disease, namely, carcinoma in both sexes, and benign hypertrophy of the prostate in males. Stricture of the ureter is no exception to this statement. One is generally accustomed to think of stricture of the ureter as a disease that occurs only in the adult. This, no doubt, is caused by the lack of study, by the physician's not being on the lookout for these cases, and also because of the scarcity of the literature on this particular subject. One of the disputed points in regard to etiology is that a large number of these cases have been reported as congenital in origin. No doubt, when a fuller knowledge obtains through careful study, it will be found that they are not all congenital in origin.

Bottomley was able to collect reports of twenty-five cases that occurred in children under 5 years of age. His patients were nearly all seen at autopsy, and while a few of them died from intercurrent disease, most of them died as the result of a lesion of the urinary tract. As is well known, these cases are always associated with hydronephrosis. Bugbee [17] affirms, as the result of his recent investigations, that less than one-third of the infants who had hydronephrosis lived more than six months. The gravity of this lesion being so decidedly evident, the importance of its early diagnosis and treatment is beyond dispute. The symptoms fall into one or two groups, as reported in a previous publication.[35]

1. In instances in which there is interference with drainage, there is renal retention resulting in the development of a tumor in the flank. When infection supervenes, chills, fever and sweats are often present.

2. In the second group there is no interference with drainage, and the patient is generally sent to the hospital with a diagnosis of acute pyelitis.

35. Kretschmer, H. L.: Surg. Gynec. Obst. **41**:713 (Dec.) 1925.

Here, as in the adult, following the passage of the ureteral catheters, there may result an interference with drainage which sometimes is followed by chills, fever and sweats, with a tumor in the flank and clear and sparkling urine.

### DIVERTICULA OF THE BLADDER

In two of these cases diverticula of the bladder were found. These did not differ in any way from the diverticula encountered in the adult, and the patients were treated surgically in the usual way, namely, by diverticulectomy. Both cases were associated with a contracted neck of the bladder, which was treated by resection at the same time that the diverticula were removed.

### OBSTRUCTION OF THE VESICAL ORIFICE

Obstruction at the vesical orifice in the adult is a well-recognized clinical entity, but its occurrence in infancy and childhood has been rather neglected in the literature as far as I know. The publications of Beer [31] and Hyman [36] of New York are the most recent and the most extensive and complete, as far as I know.

In this series there are three in which obstruction at the vesical orifice was found. In two of them the obstruction was caused by fibrous contracture of the internal urethral orifice. In one case the obstruction was associated with a stricture of the right ureteral orifice, resulting in its enormous dilatation and prolapse of the ureter, so that the prolapsed ureter covered the internal urethral orifice. This, in turn, caused an obstruction and a large amount of residual urine.

### TUMORS OF THE BLADDER IN THE YOUNG

The occurrence of tumors of the bladder in relation to tumors of other organs has been estimated as varying from 0.39 to 0.76 per cent. The occurrence of tumors in infants and children is rare. According to case reports in the literature, the prognosis is exceedingly grave and the termination nearly always fatal. The literature on this subject is meager and consists, for a large part, of single case reports, although in Europe certain compilations or dissertations have appeared. In this country only two papers are familiar to me, one by O'Neil [6] of Boston and another by Deming of New Haven.

Deming [32] was able to find only sixty-four cases in the literature, to which he added two of his own. While epithelial tumors are common in the adult, they are rare in children. On the other hand, mesothelial tumors are rare in adults but common in children. Table 6 (Deming) shows the form of tumors of the bladder occurring in the first decade of life.

36. Hyman, A.: J. Urol. **16**:259 (Oct.) 1926.

The symptoms do not differ materially from those present in connection with tumors in adults; namely, hematuria and distress of urination. Koll [37] reported an unusual and interesting polyp of the urinary bladder in an infant 13 months old.

In this series one tumor of the bladder was found in a patient, aged 7 years, who had angioma in the dome of the bladder.

### MALIGNANT TUMORS OF THE KIDNEY

Malignant tumors of the kidney in children are rare. As a rule, they grow rapidly and because of the rapid growth they cause the death of the patients at an early date. They occur with great predilection in the first five years of life and are not commonly found after the eighth year. Steffen found 168 in 219 cases, in the first five years of life; 134 of these occurred in the first year and fifty-five in the second. There is apparently no difference in the occurrence in the sexes. One of the characteristics of malignant tumors of the kidney is the rapid rate of growth and the fact that in the early stage the tumors are

TABLE 6.—*Tumors of the Bladder Occurring in the First Decade of Life*

| | Number of Cases | Percentage |
|---|---|---|
| Sarcoma | 37 | 56.9 |
| Myxoma | 16 | 24.5 |
| Fibroma | 5 | 7.6 |
| Rhabdoma | 2 | 3.0 |
| Polyp | 2 | 3.0 |
| Dermoid | 1 | 1.5 |
| Papilloma | 1 | 1.5 |
| Myoma | 1 | 1.5 |

practically symptomless. It is probably true that in the large majority of cases, the tumors are discovered by accident. The parents are the first to notice the large size of the abdomen and bring the patient to the physician. The fact that the mixed tumors occur more frequently that hypernephromas in children is recognized by all authorities. In this series there are three patients who had malignant tumors, one 3 years and two 6 years of age. Here, as elsewhere, the single agent that gives the most information is, of course, the pyelogram, which, as already stated, is feasible in the extremely young.

### TUBERCULOSIS OF THE KIDNEY

Tuberculosis of the kidney in infancy and childhood has not received much attention in the literature. It is generally believed that renal tuberculosis occurs with the greatest frequency during the period of adolescence. As a matter of fact, this is true, but it is my impression that as this phase of pediatrics receives more and more careful study, more and more cases of renal tuberculosis will be found in infancy and

37. Koll: Ann. Surg., November, 1911.

childhood, thereby establishing the fact that, after all, renal tuberculosis does occur at a much earlier period in life than is believed at the present time.

Of the eighty-six cases in this series of urologic conditions in infancy and childhood in which cystoscopy and ureteral catheterization were carried out, five patients had tuberculosis of the kidney, and in three of the five, or 60 per cent, the condition was bilateral. This, in my opinion, is a high incidence. Of course, five cases is a small number from which to draw conclusions regarding renal tuberculosis. It may be that this is merely a coincidence, and that it does not represent the true status of tuberculosis in infancy and childhood. I believe, however, that it is well to bear in mind the possibility of this condition, and to examine thoroughly all infants and children who have renal pyuria, so as not to overlook renal tuberculosis.

### CONGENITAL VALVES IN THE DEEP URETHRA

Obstruction to urination due to the presence of congenital valves in the deep urethra is a clinical entity that generally is looked on as being rare. The literature on this subject is exceedingly rare. Young, Frontz and Baldwin [38] reported an interesting case on this subject several years ago, and recently Frontz, from the same clinic, has published a paper based on a series of fifteen cases in which a diagnosis of urinary obstruction, resulting from congenital urethral valves, was made. He calls attention to the fact that unless these obstructions are seen early and relieved early, serious injury to the upper urinary tract will result. Perhaps the majority of these obstructions may be caused by congenital valves or by a lesion of the nerve resulting from spina bifida. The degree of obstruction from congenital valves varies. The obstruction may be so complete that death occurs after a few years of life, or patients may reach adult life with few symptoms.

In this series there is a boy, aged 12, on whom a diagnosis of congenital valves was made. Recently, Ehrich [39] reported an interesting case of this type, and several cases have been reported by Lansdowne and Boyd.[40] They report a most interesting series of cases of so-called congenital dilatation of the ureters due to congenital valves in the posterior urethra and one case doubtless due to a spina bifida.

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38. Young, H. L.; Frontz, W. A., and Baldwin, J. C.: J. Urol. **3**:289 (Oct.) 1919.

39. Ehrich, W. S.: J. Urol. **13**:471 (April) 1925.

40. Lansdowne and Boyd: Canad. M. A. J. **15**:361 (April) 1925.

### URINARY LITHIASIS

Thomas and Tanner,[41] who collected a series of 203 cases of urinary lithiasis in infancy and childhood (155 boys and forty-five girls, a ratio of almost 3:1), believe that this condition occurs much more frequently than is generally supposed since many cases are not recognized, especially those in which a large number of stones are passed after an attack, supposedly of intestinal colic.

In the series reported, there were seven cases of lithiasis distributed as shown in table 7.

In several instances the bladder stones were treated by litholapaxy, in a manner similar to the method pursued when this condition obtains in the adult.

A matter of interest is the fact that the various diagnoses made in this series of cases correspond closely with those based on similar lesions found in the adult, so closely, indeed, that one is justified in stating that the lesions and symptoms are alike in both adult and infant. One point to note in this series is that the lesions of the kidneys outnumber to a considerable degree those of other organs, since half of the cases were of renal origin.

TABLE 7.—*Distribution of Cases of Lithiasis*

| | Number of Cases |
|---|---|
| Kidney | 1 |
| Ureter | 2 |
| Bladder | 4 |

### SUMMARY

1. Urologic problems in infancy and early childhood resemble similar problems in the adult.

2. The technic can be mastered with practice, and once the operator becomes expert with the small instruments, no difficulties will present themselves.

3. At the present stage of advancement in medical knowledge, procrastination, in place of careful and complete urologic study in all cases that do not promptly respond to treatment, has not the shadow of an excuse.

4. Instrumental therapy, by which is meant lavage in pyelitis and litholapaxy in the treatment of stones in the bladder, can be carried out with the same precision as in adults.

5. The surgical treatment of the various lesions encountered presents no special problems.

41. Thomas and Tanner: Minnesota Med. **5**:147 (March) 1922; J. Urol. **13**:171 (Aug.) 1922.

# News and Comment

## DEATH OF PROFESSOR GOEPPERT

On February 9, at the age of 56 years, Professor Friedrich Goeppert died. At the time of his death Dr. Goeppert was professor of pediatrics at the University of Gottingen. He contributed largely to pediatric literature and was especially well known for his articles on practical subjects.

## TRAINING FOR SIGHT SAVING

Summer session in courses for the training of teachers for sight saving classes are being given this summer at the University of Southern California, University of Cincinnati, Western Reserve at Cleveland and at the Ohio and Peabody College at Nashville, Tenn.

# Obituary

## HENRY KOPLIK, M.D.

1858-1927

Henry Koplik was born, Oct. 28, 1858, and died April 30, 1927, in his sixty-ninth year. All his living days were busy ones, chiefly devoted to the study and practice of disease in children. He established the first sterilized milk depot for infants in this country at the Good Samaritan Dispensary. This milk depot was a pioneer movement, which is now an established custom in our larger cities. He was the author of a textbook, "Diseases of Infancy and Childhood," and also wrote numerous monographs and articles pertaining to his specialty. For twenty-five years, he was the attending pediatrician of Mount Sinai Hospital of New York, where he organized a modern children's pavilion.

His discovery in 1896 of the buccal spots of measles, now known all over the world as Koplik spots, was undoubtedly his greatest claim to fame. He was the first to grasp the significance and diagnostic import of this sign. Its diagnostic interpretation was quickly recognized by pediatricians, both national and international, and was promptly incorporated in the textbooks under the name of Koplik spots. From then on honors were heaped on him, both in this country and abroad. He was one of the founders of the American Pediatric Society, a member of the Association of American Physicians and of the Permanent Committee of Child Welfare, as well as of other national and international societies. His opinion on all pediatric questions was eagerly sought. In epidemics of diseases peculiar to children, he always was consulted by the New York Health Department and was placed on committees for investigating the diseases. He was for years a popular consultant, not only in practice but also in various institutions.

As a man, his dignity and proper regard of professional position were his outstanding features. He labored to put the practice of medicine and society in general on a higher plane. He never looked down, always up; yet he could be as kindly and generous as any man. He took a particular pride in instructing and educating young mothers in the ways and manners of their infants. His finest quality, perhaps, was his indomitable will, which forced him to fight for what he thought was right. His discovery of the Koplik spots alone would have won for him a permanent place in the history of medicine.

H. H.

# Abstracts from Current Literature

## Anatomy and Physiology

LIPOIDS AND PIGMENT IN THE UPPER RESPIRATORY MUCOSA. H. MITSUHASHI, Virchows Arch. f. path. Anat. **261**:1, 1926.

As a contribution to the normal and pathologic distribution of lipoids in human tissues, Mitsuhashi, at the suggestion of Lubarsch, investigated the occurrence of lipoids and pigment in the mucosa of the nose, larynx and trachea in 200 patients varying in age from fetuses to the seventieth year. At all periods adipose tissue is present in the mucosa in the situations studied, except in the nose. In the normal mucosa of children and adults phosphatids are present in the cells of the mucous glands. These phosphorus-containing lipoids increase in chronic metabolic disease and in diseases associated with cachexia. They are not increased in tuberculosis if cachexia is absent. In local inflammatory conditions the macrophages contain anisotropic phosphatids. Metabolic pigment appears early in life in the smooth muscle cells and increases with age. It becomes greater in amount in chronic metabolic and cachectic diseases but the increase is not parallel to that of the phosphatids in the same conditions. The intracellular formation of lipoids in vitro in the explanted respiratory mucosa of the rabbit was found to be dependent on the composition of the medium.

PATHOLOGIC ALTERATIONS OF ARTERIES OF THE UPPER EXTREMITY. MARGARETE HESSE, Virchows Arch. f. path. Anat. **261**:225, 1926.

Margarete Hesse, working in the laboratory of Anitschkow, who has devoted much of his attention to arteriosclerosis, made a systematic study of the arteries of the upper extremity, from the subclavian to the radial artery, in forty-one necropsies of subjects varying in age from 2 days to 79 years. A normal gross anatomic characteristic of the portion of the arterial system studied is the transformation of the thicker, elastic type of artery into the thinner, muscular type at the level of the superior border of the pectoralis major muscle. At the region of the elbow the brachial artery is normally somewhat wider than just above this situation, its course is more tortuous, its wall is less elastic and its intima is somewhat uneven. The media here is usually richer in ground substance and connective tissue than elsewhere and many of the muscle fibers do not take an even, circular course. In younger persons the length of the main arterial stem of the upper extremity underwent a shortening of about 40 per cent of its length on removal, whereas in older persons the shortening was slight. Atherosclerotic changes characterized by fatty change but without calcification were almost the rule in the subclavian and axillary subdivisions in persons above the fourth decade. Beyond the point of transition of the vessel from the elastic to the muscular type lipoid infiltration was only slight, localized calcified plaques were rare, but diffuse calcification of the media was much more marked and increased distally, being greatest in the radial and ulnar divisions.

O. T. SCHULTZ.

THE TOPOGRAPHY OF THE BRONCHIAL LYMPH NODES AND THEIR ANATOMIC DEMONSTRATION. S. ENGEL, Beitr. z. Klin. Tuberk. **64**:468, 1926.

A careful anatomic study led to the establishment of the following groups of lymph nodes: (1) lymphoglandulae bifurcationis dexter et sinister; (2) lymphoglandulae tracheobronchiales dexter; (3) lymphoglandulae hilares anteriores dexter; (4) lymphoglandulae hilares posteriores dexter (interlobares); (5) lymphoglandulae hilares anteriores sinister; (6) lymphoglandulae hilares posteriores sinister (interlobares); (7) lymphoglandulae aortae; (8) lymphoglandulae ductus botalli.

MAX PINNER.

## Pathology, Bacteriology and Biochemistry

HEPARIN INHIBITION OF ANAPHYLACTIC SHOCK. PRESTON KYES and E. R. STRAUSER, J. Immunol. **12**:419, 1926.

In pigeons the intravenous injection of 1 cc. of a 1 per cent solution of heparin forty-five minutes before the injection of the second or critical dose of sheep serum practically eliminates all symptoms of anaphylactic shock. As heparin inhibits fibrin formation, it is suggested that there is "a causal relation between fibrin emboli and the symptoms of shock."

[ARCH. PATH.]

THE BIOLOGY OF OÏDIUM ALBICANS, WITH SPECIAL REFERENCE TO MYCELIAL PRODUCTION. A. A. DRAPER, J. Infect. Dis. **39**:261, 1926.

Yeasts of *Oïdium albicans*, when grown in carrot infusion, developed as mycelia below a certain level in the test tube. The ash of carrots contained some substance that influenced such mycelial growth. Analyses of the ash showed that it contained a large amount of phosphorus.

Various phosphate containing salts, in appropriate concentrations in 1 per cent peptone solutions, supported the hyphae growth.

The organisms grew as mycelia in meat infusion agar if a small amount of inorganic phosphate or carrot infusion was added, and special partial tension conditions were maintained.

Various strains of the organism differed in their biochemical and physiologic activities. Cells of the same strain when grown in different phosphate mediums developed type colonies that were specific for their respective mediums. Three such types were observed.

A type grown in its specific medium over a considerable period of time did not retain its type characters when transplanted into a medium specific for another type.

Exposure of cells from a given type colony to an appropriate amount of heat tended to fix the type colony characters to the extent that they were retained when they were seeded in a medium which usually supported another type. By this method type 1 was fixed on iron phosphate ($Fe\ PO_4.4H_2O$) medium, and type 2 was partially fixed on carrot infusion medium. The degree of permanence of this fixation has not yet been determined.

AUTHOR'S SUMMARY.

CALCIUM METABOLISM IN DISEASE. C. P. STEWART and G. H. PERCIVAL, Edinburg M. J. **34**:95 (Feb.) 1927.

This is a critical review of the literature, with summaries of reports from numerous authors on the blood calcium content in rickets, tetany, nephritis, diabetes, eclampsia, jaundice, pneumonia, epilepsy, syphilis, pulmonary tubercu-

losis, atheroma and hypertension, arthritis, gout and skin and other diseases. The bibliography is extensive, comprising 130 citations.

NEFF, Kansas City.

IMPENDING ACTION OF ULTRAVIOLET RAYS IN EXPERIMENTAL VACCINATION OF RABBITS. P. CARNOT, L. CAMUS and H. BENARD, Compt. rend. Soc. de biol. **95**:457, 1926.

Rabbits previously irradiated by ultraviolet rays were infected with vaccine. The experiments led to the conclusion that a preliminary irradiation by ultraviolet rays renders the rabbit's skin refractory to the vaccinal eruption. The action is essentially local, since in areas not irradiated cutaneous lesions did appear.

B. M. FRIED.

PROTEIN TOXICOSIS. L. A. TSCHERKES, Biochem. Ztschr. **182**:35 (Feb. 25) 1927.

White mice on an exclusively protein diet develop an acute toxicosis and die in from one to five days. The intoxication is not due to starvation or avitaminosis. Addition of fat or carbohydrate to the diet decreases the intoxication. Rats and doves developed a similar intoxication on an egg albumin diet but not on a casein diet.

M. B. BRAHDY, New York.

RESEARCHES ON THE EXCRETION OF ACID IN THE URINE OF CHILDREN. III. FURTHER OBSERVATIONS ON THE QUESTION OF THE EXCRETION OF ORGANIC ACIDS. JOACHIM BROCK, Ztschr. f. Kinderh. **41**:378, 1926.

The connection between the excretion of organic acids in the urine and the metabolism of albumin has been studied by the author on the basis of new examinations. The relation of the two factors is not dependent on albumin intake but on albumin exchange, as appears in the determinations of the urinary nitrogen. High values for albumin exchange, from 0.4 Gm. of nitrogen up, per kilogram of body weight, were accompanied by evidence of influence on the excretion of organic acid, and usually in the way of a sudden climb above a high level. This result was found also in a piece of work carried on for more than six weeks on an adult in whom the urinary nitrogen varied from 5 to 50 Gm. Although the albumin exchange of the adult on a mixed diet rich in meat did not exceed 0.25 Gm. of nitrogen per kilogram of body weight, the dependence of the excretion of organic acid on albumin metabolism had theoretical interest, the organic excretion calculated on the basis of body weight per kilogram, having been somewhat the same as in breast-fed infants —that is, 6.4 cc. of $\frac{1}{10}$ normal acid. Practically, in relation to the pathologic changes of infants, the acidotic activity of a high albumin exchange was important, because exchanges above 0.4 Gm. of nitrogen are the order of the day in modern artificial feeding.

In general, the increase in the excretion of organic acids thus induced appears higher in infancy than in older children and in adults, and may amount to more than 100 per cent.

Corresponding to the view of Freudenberg and György, the children with rickets fed in the usual way sometimes show a much increased excretion of organic acids, which does not occur in cases showing spasmophilia, and sometimes show when fed on a diet with excessive fat, an acidosis with organic acids in connection with a ketonuria. In healthy children on a diet with excessive fat, there could not be demonstrated an acidosis with organic acids, even if the reaction was pushed in the acid direction.

As regards laboratory technic, the error in carbonate found by Budde with the Van Slyke-Palmer method for the determination of organic acids was studied, its slight significance shown, and a simple supplement to the original method given, which completely eliminates the error.

THE UREA CONTENT OF SALIVA IN INFANTS AND CHILDREN. C. FALKENHEIM, Ztschr. f. Kinderh. **41**:530, 1926.

The Hench and Aldrich method of determination of urea in saliva is suitable with some slight modifications for use in the infant. The normal value is lower in infants than in children and in adults:

From 6 to 44 mg. per cent in infants.
From 12 to 64 mg. per cent in children.
From 30 to 82 mg. per cent in adults.

The age and condition of nutrition of the infant appeared to be without significance. High normal values in resolving pneumonia and fresh empyema were found, due to the flushing of the organism with the products of the breakdown of albumin.

EMERSON, Boston.

## Nutrition

THE EFFECT OF VARIATIONS IN PROTEIN INTAKE ON THE ACIDITY OF THE SECRETION OF THE FASTING STOMACH. F. HOELZEL, Am. J. Physiol. **77**:166, 1926.

Of principal interest was the discovery, in a human subject, that excessive protein in the diet caused a decrease in the acidity of the secretion of the fasting stomach. A wide range of proteins proved effective in this connection. From this, and from the fact that functional rest, either by fasting or by protein restriction, was followed by an increased acid secretion, it is suggested that the phenomenon is one of secretory fatigue, and that this fatigue may play a part in the natural regulation of protein intake in food.

H. E. EGGERS.

EFFECT OF THE CALCIUM, VITAMIN C, VITAMIN D RATIO IN DIET ON THE PERMEABILITY OF INTESTINAL WALL TO BACTERIA. AGNES H. GRANT, J. Infect. Dis. **39**:502, 1926.

An adequate balance between dietary calcium, vitamin C and vitamin D is essential in maintaining the normal resistance of the intestines to the migration of intestinal bacteria into the blood stream.

A severe disturbance in the proper ratio between vitamin C and vitamin D increases the permeability of the intestines to bacteria. This is true both when there is an excess of vitamin D and a deficiency of vitamin C, and when there is an excess of vitamin C and a deficiency of vitamin D.

The oxidation of cod liver oil destroys its content of vitamin A, but it does not destroy the factor that is responsible for the marked decrease in intestinal resistance.

Oxidizing the orange juice destroys its power to inhibit the factor in cod liver oil that is responsible for the marked decrease in intestinal resistance due to the cod liver oil factor.

An excess of calcium seems to favor the migration of bacteria into the blood stream whenever used; and when vitamin C and vitamin D are both deficient, it seems to favor a rapid multiplication of the bacteria in the spleen and lungs.

AUTHOR'S SUMMARY.

THE PREVENTION OF POOR APPETITE IN CHILDREN. C. A. ALDRICH, The National Committee for Mental Hygiene, Inc., Reprint 220, New York, N. Y., 1927.

Recognizing the seriousness of chronic anorexia in childhood and the difficulties attending its cure, Dr. Aldrich has turned his attention to prevention. He feels that the condition develops in two stages. First, a readily understandable physical or mental cause results in lack of appetite. Food forced at this time when it would be better withheld fixes on the child a psychologic aversion to food, and further continued urging only strengthens this.

For more than five years the author has instructed the mothers of his patients never to urge their children to eat, when a child refuses food to reduce immediately the amount of food offered, to accustom the child gradually to changes in food and to leave him alone at meal time. The questionnaire showed that among 199 children whose parents had been so instructed, 85 per cent ate hungrily or willingly as against 19 per cent in an unselected group. The children averaged 3.6 pounds overweight; only eleven were underweight, and there were no malnourished children in the group except those who were suffering from a chronic disease.

LESLIE, Chicago.

THE GROWTH OF NORMAL INFANTS IN CAGLIARI. ATTILIO MACCIONI, Riv. di clin. pediat. **25**:1, 1927.

The author has gathered data regarding the size of 220 normal new-born infants in Cagliari, Sardinia, and has obtained monthly measurements of sixteen of these throughout the first year.

The conclusion is reached that at birth the infants of Cagliari are of equal or greater size than infants from Italy, but they tend to become relatively smaller as they develop. Racial peculiarities are manifest in the first year of life.

HIGGINS, Cincinnati.

THE LIVER IN NUTRITIONAL DISTURBANCES. R. GRALKA and W. REINOLD, Jahrb. f. Kinderh. **115**:127 (Feb.) 1927.

A study was made of the livers of patients who died with keratomalacia and other nutritional disturbances. The fat was extracted with alcohol and then with ether. The amount of fat in the liver was in direct proportion to the severity and duration of the nutritional damage to the organism. The alcohol extract consisted of lipoids and the ether extract of cholesterin, lecithin, and neutral fat. The decrease in vitamins during disease is reflected in the diminished fat content of the liver.

PETERMAN, Milwaukee.

INFECTIOUS DIARRHEAS IN INFANCY. OSCAR HERZ, Monatschr. f. Kinderh. **35**: 193, 1927.

Since milk is universally boiled, infectious diarrheas have become relatively rare. That they do occur is shown by the author's report of forty-five cases occurring during 1925 and 1926. The origin of them is uncertain although it is suspected that the infection was spread in the wards by doctors and nurses. The bacteriology was indefinite. No specific organism was found. The gross appearance of the stools, however, was characteristic, being typically blood and mucous. The duration of the diarrhea was from ten to fourteen days. The temperature was inconstant, varying from subnormal to 105. Of the forty-five patients only two died, this mortality being much lower than in true dysentery.

Most of the infants were under 6 months, and previous breast feeding did produce immunity. The epidemic started suddenly, all infants in one ward sickening the same day. The only organisms found were colon bacilli and hemolytic streptococci. In the treatment, the author got the best results by giving a minimum of 100 calories per kilogram. He warns particularly against the dangers of hunger.

There were two such epidemics in the institution occurring during the month of June through September.

CONCERNING THE DEMONSTRATION OF VITAMIN RESERVES IN THE HUMAN ORGANISM. PETENYI, Monatschr. f. Kinderh. **35**:252, 1927.

In previous studies, Petenyi has shown the potato to be rich in a water soluble vitamin. He now reports three cases of children who were not gaining. The addition of a small amount of potato produced an immediate gain in weight, which lasted some time after the potato was stopped. When the weight curve straightened out, the addition of small amounts of potato produced a resumption of the upward curve. The author concludes that water soluble vitamin can be stored in the body, and in the human organism he believes that he has shown experimentally that the duration of the storage may be a number of months. Possibly on a given diet we may be able to estimate the amount of vitamin necessary daily.

GERSTLEY, Chicago.

STUDIES IN RICKETS. E. FREUDENBURG and A. WELCKER, Ztschr. f. Kinderh. **41**:466, 1926.

Up to this time research in rickets has been concerned with the influence of inorganic substances, but apart from vitamins, organic foodstuffs must have some influence. This is probable from several bits of evidence: (1) the increase of urinary ammonia when carbohydrate has been withdrawn from the diet and the fat increased; (2) an increase in the urine of organic acids, and in this connection comes a consideration of the patients with rickets who have been overfed with milk; (3) the susceptibility of patients having rickets to acidosis. This piece of evidence is significant because the disturbance in antiketogenic power may be dependent on a disturbance in the breaking down of carbohydrate, which cannot be explained by a slowing of the metabolism of carbohydrate or by a change in the oxidation of sugar. It might be explained by a checking of the anaerobic phase of the breakdown of sugar called glycolysis.

The author has shown that in the blood of children with florid rickets glycolysis is diminished and often completely arrested. In incipient rickets, the diminution of glycolysis is not so definite as it is in fully developed cases. In spasmophilia, on the other hand, there is an active glycolysis in the blood. The diminution of glycolysis may be explained (1) as a result of the increased destruction of hexose-phosphate to sugar and phosphate by the ferment phosphatase, and (2) as a result of excessive resynthesis of sugar from lactic acid.

That these changes occur in the tissues as well as in the blood may be suspected from the evidence that a higher hydrogen ion concentration in the tissues and an increased formation of acids are present. Glycolysis depends greatly on $p_H$. Hypophosphatemia in dogs has been shown to occur with a lack of phosphate in the liver. The normal process of breaking down carbohydrate is dependent on the assistance of phosphorus of which it is probable there is a

general deficiency. An abnormally low formation of lactic acid is present in the tissues, and as lactic acid must be due to glycolysis, there must be glycolysis in the tissues. The arresting of glycolysis in the blood, hypophosphatemia and hypolactacidemia is a triad that goes along with a retarded metabolism in rickets, and on the other hand, these factors are all normal or above normal with the increased metabolism in spasmophilia.

Under treatment with sunlight and vitamins, it has been shown by the author that the blood regains its power of glycolysis in rickets. The question used to be in this disease, "Why are not the bones calcified?" The question now is "How does it come about that without sunlight and vitamins hypophosphatemia arises?"

EMERSON, Boston.

BASAL METABOLISM AT THE AGE OF PUBERTY. H. LAX and G. PETENYI, Orvosi hetil. **71**:202, 1927.

Determination of basal metabolism was performed in thirty children, mostly girls. The results show that basal metabolism in more than half of the cases is considerably increased. The specific dynamic reaction of Kestner and Plaut was diminished or absent in a great majority of the cases. Therefore, this reaction cannot be used as a diagnostic sign of disturbances of the hypophysis.

BASAL METABOLISM IN ADIPOSE CHILDREN AT THE AGE OF PUBERTY. H. LAX and G. PETENYI, Orvosi hetil. **71**:228, 1927.

In fourteen adipose children, basal metabolism was determined with Krogh's gas apparatus. The specific dynamic reaction of Kestner and Plaut was determined in twelve cases. The results show that basal metabolism of adipose children of adolescent age is decreased. The normal increase of basal metabolism seen in puberty is absent in these cases. The specific dynamic reaction of Kestner and Plaut cannot be used for differentiating the hypophysial forms of adiposity from the other cases.

ZENTAY, St. Louis.

## Prenatal Conditions

A MICROHYDROANENCEPHALIC ANARIC ANCYCLOPIC MONSTER. H. H. SKINNER, M. J. & Rec. **125**:16 (Jan. 5) 1927.

This monster was a male child born of healthy parents. He weighed 10 pounds (4,535.9 Gm.) at birth and lived eighty-one and one-half hours. There were five healthy brothers living. When first seen, the infant was markedly cyanotic and had great difficulty in breathing. The general appearance of the head was that of a microcephalic infant. There was no eye socket, but on palpation a small one could be found which seemed to be a fused union of the usual two on the upper edge of which was an eyebrow. Below this were the lower lids of two eyes with a common canthus. From here to the upper lip was merely a skin surface. No nose could be discovered by deep palpation or observation.

There were evidences of faulty closure of the branchial clefts. Otherwise the infant was well developed, well formed, strong and healthy.

The article is accompanied by photographs of the abnormalities and roentgenograms of the head. A report of the autopsy is also given.

FACIAL ASYMMETRY. P. G. BROWN, Proc. Roy. Soc. Med., December, 1926, vol. 20.

A boy, aged 11 years, showed marked facial asymmetry. The right eye was at a lower level than the left. There was much bony overgrowth of the right frontal region. Eye movements were normal, and there was no diplopia. The fundi were normal; roentgen-ray examination showed: apparent lack of development of the right side with marked thickening of the right frontal area of the skull extending back to the pituitary fossa which was small and bridged. The condition did not give the appearance of true tumor.

WILLIAMSON, New Orleans.

FAMILIAL CONGENITAL MALFORMATIONS. OTTO HILDEBRAND, Monatschr. f. Geburtsch. u. Gynäk. **75**:32 (Nov.) 1926.

There was an hereditary influence in 207 of 385 cases of harelip. There were three cases in one family in which the father also had a harelip.

PETERMAN, Milwaukee.

STATISTICAL REPORTS ON PREMATURE INFANTS. A. ISRAEL and B. KEMKES, Monatschr. f. Kinderh. **35**:289, 1927.

During the years 1914 to 1925, there were 902 premature infants at the university clinic. The authors accept Ylppö's definition of a premature infant; namely, any child under 2,500 Gm. Full-term children of this weight were not included.

The number of premature infants almost doubled during 1918 and 1919, and this increase was greater than the increase in the general birth rate. No explanation is offered, unless possibly criminal and social conditions were responsible. The season of the year had no apparent effect. In this respect, the authors also found no relation between the season of the year and the size of the infant. They cannot confirm the statements of others that children born during the warmer months are larger than those born during the colder months. As regards sex, there were 107 boys to 100 girls. In general, however, since the war, there has been a relative increase in the birth rate of boys.

Classified according to weight, there were 7.2 per cent under 1,000 Gm., 26.4 under 1,500 Gm., 42.2 under 2,000 Gm. and 24.2 under 2,500 Gm. As regards mortality, children under 1,000 Gm. showed 98.5 per cent, under 1,500 Gm. 83 per cent, up to 2,000 Gm., 48 per cent, and up to 2,500 Gm., 35 per cent. Mortality by sexes gave 54 per cent for girls and 61 per cent for boys. The mortality of illegitimate children averaged 55 per cent against 45 per cent of those born in wedlock. The authors cannot explain this, as there was no difference in the death rates of the full-term children of either class.

The prognosis depends on the infant's weight and clinical reactions.

Premature infants show less physiologic loss of weight relatively than full-term children, and regain their birth weight somewhat more rapidly.

None of the infants were placed in incubators.

The authors conclude the article by calling attention to the difference in statistics which may result from their originating in a lying-in hospital or a children's hospital. The lying-in hospital can give the absolute number, while the children's hospital can report on only those who come to it living.

GERSTLEY, Chicago.

Pathogenesis of Congenital Hydrops. G. Nordmann, Zentralbl. f. Gynäk. **50**:2945 (Nov. 13) 1926.

The causes of congenital hydrops are: (1) diseases due to malformations of the heart and great vessels, or a superimposed endocarditis; (2) toxemia resulting from maternal disease; (3) congenital syphilis; (4) hyperplasia of the lung, lung tumor or accessory lung tissue. A case of congenital hydrops is reported in which death ensued immediately after delivery. There were no signs of syphilis. There was an accessory left lung, which was not connected with the bronchial tree. Hydrops was apparently due to the mechanical disturbance of the circulation.

Atresia of the Esophagus with Congenital Varicosities and Tracheal Fistula Simulating the Clinical Picture of Melena Neonatorum. E. Noltman, Ztschr. f. Geburtsh. u. Gynäk. **110**:260 (Nov.) 1926.

Noltman reports the necropsy in a twin weighing 6 pounds (2,727.5 Gm.), apparently normal at birth, which had hematemesis and melena from twenty-four hours after delivery until its death five days later. He found atresia of the esophagus at about its middle and several varicosities in the mucosa. There was a fistula leading from the esophagus to the bifurcation of the trachea. There was an exudation of blood in the meninges over the temporal lobes, and in the ventricles. Patches of aspiration pneumonia were found in the right upper lobe. The ejection of ingested material was probably initiated by an irritation in the trachea by food or blood from the esophagus.

M. B. Brahdy, New York.

## Diseases of the New-Born

The Problem of Fetal and Neonatal Death. E. B. Sterling, Public Health Reports 42, no. 11 (March 18) 1927.

From a study of statistics in the birth registration area of the United States from 1916 to 1924, it is clear that although the total infant mortality rate had fallen considerably (30 per cent) there had been little change in the fetal and neonatal mortality. If further advance is to be made, a more complete knowledge of the causes of fetal and neonatal death is necessary. So far, syphilis is the only one of which there is sufficient knowledge to hope for marked success in its prevention. Birth injury and prematurity rank highest as the causes of death in this group, but relatively little is known of the causes of the dystocia or of prematurity. In addition to work along these lines, the author suggests that a special study should be made of the infections of the new-born.

Leslie, Chicago.

Emphysema in Asphyxiated New-Born Infants. Ernest Poeck, Monatschr. f. Geburtsh. u. Gynäk. **74**:341 (Oct.) 1926.

Two cases of fatal emphysema in new-born infants are described. In one case, the pericardium was also distended with air. In this case, forced artificial respiration was held responsible for the death. Compression and manipulation of the chest may have been responsible for the second fatality, although both infants were cyanotic at birth.

Peterman, Milwaukee.

MENINGITIS IN THE NEW-BORN. DORA KARPLUS, Wien. klin. Wchnschr. **40**:250 (Feb. 24) 1927.

Karplus reports three fatal cases of meningitis in infants less than 4 weeks old. Two were due to staphylococci that had reached the meninges by direct extension from an infected spina bifida. Only one of the patients had been operated on. The third case was caused by meningococcic infection, the patient dying on the twenty-fourth day of illness in spite of specific therapy. The author reviews thirty-seven reported cases of neonatal meningitis. Infection is usually hematogenous in origin. It may, however, extend directly or by way of the lymphatics from contiguous foci (infected ear, sinus, orbit, nose or mouth). Thirty per cent of the cases are due to *B. coli*, the meningitis being part of a general sepsis. Infected amniotic fluid or bath water, maternal metritis, the placing of the obstetrician's fingers in the infant's mouth, etc., have been offered as explanations for infection with *B. coli*, but Karplus does not think the evidence conclusive. Staphylococcus and streptococcus are responsible for 32.5 per cent of the cases and pneumococcus and meningococcus each for 10 per cent. Neonatal meningitis due to the tubercle or the influenzal bacillus has never been reported.

The common symptoms found in older children (fever, rigidity, signs of increased intracranial pressure, etc.) are often lacking in meningitis of the newborn. Coma, increased or decreased sensibility, or a staring countenance may be the first symptom to suggest examination of the spinal fluid.

OLMSTEAD, Seattle.

## Acute Infections

FURTHER STUDIES ON STREPTOCOCCI FROM SCARLATINA, ERYSIPELAS AND PUERPERAL FEVER. G. H. EAGLES, Brit. J. Exper. Path. **7**:286, 1926.

All strains of hemolytic streptococci from scarlet fever produce toxic filtrates as judged by intracutaneous tests. A large number of strains from erysipelas, puerperal fever and various other pathologic conditions produce a similar toxic filtrate. All toxic filtrates, regardless of their source, are neutralized by scarlet fever horse serum. Results obtained when immune rabbit serums from various toxin-producing strains are used for neutralization may indicate, however, higher specificity. By agglutination three main groups are shown to exist among hemolytic streptococci. The scarlet fever and erysipelas groups are confirmed and a similar grouping is shown among strains from puerperal fever. Toxin production and agglutination by scarlet fever immune serums are not closely related when strains from a variety of pathologic sources are studied.

S. A. LEVINSON.

SOME CONSIDERATION ON "LA FIEVRE GANGLIONNAIRE." P. GAUTIER, Rev. franç. de pediat. **2**:475, 1926.

The fever associated with malaise, enlargement of the cervical lymph glands and a slight pharyngitis is the clinical entity under consideration. It has been thought by many to be associated with that indefinite group of conditions designated as grip. The author, however, feels that it is more properly related to a scarlatinal infection because of the frequent finding of the streptococcus and the similarity of the complications, otitis media and nephritis, in the two conditions.

LESLIE, Chicago.

IMMUNIZATION AGAINST DIPHTHERIA. FLORENCIO BAZÁN, Arch. latino-am. de pediat. **20**:829, 1926.

The author gave the Schick test to 1,833 children and adults varying between the age of 3 and 20 years. The material was taken from a number of charitable institutions in Buenos Aires. Of the cases tested, 38.2 per cent gave positive reactions. Immunization was carried out by injecting two doses of Ramon anatoxine—0.5 cc. and 1 cc., respectively, at intervals of from fourteen to twenty days. A Schick control test applied two months after the immunization gave 86 per cent negative reactions in the cases in which the reactions had been positive.

SCHLUTZ, Minneapolis.

PYOCYANEUS INFECTION IN INFANTS. HERMANN CHIARI, Centralbl. f. allg. Path. u. path. Anat. **38**:483, 1926.

In autopsies on three children, all about a week old and dying presumably from "toxic grippe and erythema," a meningitis and pericarditis were found due to *Bacillus pyocyaneus*. Cultures of the organism from the brain and bowel killed guinea-pigs in twelve hours and produced pyocyanase abundantly. The exudate on the brain was thickest in the frontal region and consisted of an outer layer rich in pus cells and extracellular bacilli and an inner cell-poor layer rich in fibrin. In contradiction of Fraenkel's reports the exudate was never hemorrhagic and bacilli were not found in the arterial walls. In one instance microscopic hemorrhages were found at the junction of cortex and medulla in the brain and in another bronchopneumonic foci were found in the lungs.

GEORGE RUKSTINAT.

DESQUAMATION FOLLOWING MEASLES. ALFONS REULAND, Jahrb. f. Kinderh. **115**:202, 1927.

Seventy cases were observed; in only one desquamation did not take place. The first evidences appeared from two to four days after the exanthem began and on the face. The duration was from seven to eight days. Artificial hyperemia hastened peeling.

PETERMAN, Milwaukee.

DIPHTHERIA BACILLI IN THE UPPER AIR PASSAGES OF CHILDREN WITHOUT CLINICAL DIPHTHERIA. H. KLIEWE and A. HOFMANN, Monatschr. f. Kinderh. **35**:318, 1927.

In 3,272 nurslings and small children showing no clinical diphtheria, 185, or 5.7 per cent, gave positive diphtheria cultures. Of this number, 126, or 68 per cent, of the cases showing positive reactions, or 3.9 per cent of all cases gave positive nasal cultures. Fifty-one, i. e., 28 per cent or 1.6 per cent, gave positive throat cultures. Fifteen, i. e., 8.1 per cent or 0.4 per cent, showed positive nose and throat cultures, and eight, i. e., 4 per cent or 0.2 per cent, came from the conjunctiva, the navel or the ear.

In a series of thirty strains isolated, ten were pathogenic. In a further series of eighteen, ten were nonpathogenic and eight were not tested.

The highest percentage of carriers was found in children with congenital syphilis (17 per cent). Exudative diathesis came next, with 9.2 per cent, and nutritional disturbance, with 8.9 per cent. There was no seasonal variation.

GERSTLEY, Chicago.

## Chronic Infections

GLANDULAR PULMONARY TUBERCULOSIS OF GRADUAL DEVELOPMENT IN CHILDHOOD. by PAUL LE TONDAL, The Institute Bruchesi, 1927.

A case of slowly developing ulcerative caseous tuberculosis in a child of 6½ years is presented. The cough and malnutrition, together with some gastro-intestinal symptoms, had been present for two years, and there was a definite history of exposure to tuberculosis. The author feels that there is not sufficient prevention work among children who have been exposed to tuberculosis. He suggests that when there is no evidence of infection, the children might be placed in nontuberculous families; that when a closed tuberculosis exists, they be treated in a preventorium, and for other cases, special hospitals in which the patient may be given the benefit of pneumothorax when it is necessary.

LESLIE, Chicago.

THE TUBERCULIN REACTION IN ARTICULAR RHEUMATISM AND IN ERYTHEMA NODOSUM. LUCIANO MAGNI, Riv. di clin. pediat. **25**:27, 1927.

The author observed 113 children with rheumatism (chronic, subchronic or with protracted course) and found that 79.1 per cent showed a negative tuberculin reaction. The author believes that many of these negative reactions should have been positive since (1) the children were from 10 to 12 years old; (2) there was a family history of tuberculosis; (3) there were signs of chronic respiratory infection or enlarged glands on physical examination, and (4) roentgenographic examination indicated tuberculosis. Thus, the author believes that rheumatism should be added to the list of diseases, the most prominent of which is measles, that show an "anergy" to tuberculin.

During the course of erythema nodosum, the author noticed that previous negative reactors to tuberculin became positive reactors; later tests, however were negative again.

HIGGINS, Cincinnati.

LOCAL AND GENERAL STATISTICS ON THE MORTALITY FROM TUBERCULOSIS IN CHILE. DR. A. C. SANHUEZA, Arch. Chilenos de Pediat. **3**:306, 1926.

According to the government statistics, the mortality from tuberculosis in Chile is twenty-two and in Santiago it is thirty-six per ten thousand inhabitants. These figures are not reliable, because only about 20 per cent of the deaths are reported by physicians. In the greater part of the others that are reported by laymen, many are caused by tuberculosis although not reported as such. It is estimated that one third of the deaths reported as caused by pneumonia and one fourth of those reported as caused by meningitis and convulsions are in reality tuberculous. If these were added to the present statistics, the mortality rate would be forty-four for Chile and sixty-six for Santiago per ten thousand inhabitants. These figures are contrasted with the rate of twenty-eight per ten thousand inhabitants in Paris, thirteen in Berlin, twelve in London, 8.4 in New York and 3.8 in Framingham, Massachusetts. The latter locality has done more to lower the mortality from tuberculosis than any place in the world.

Sanhueza advocates for his country, in a symposium during "Tuberculosis Week," that every death should be reported by a physician and that every case of open pulmonary or laryngeal tuberculosis should be reported to the health authorities within eight days, and every death reported within twenty-four hours.

THE CALMETTE-GUERIN ANTITUBERCULOSIS VACCINE AND ITS APPLICATION IN CHILE. DR. O. FONTECILLA, Arch. Chilenos de Pediat. **3**:312, 1926.

It is possible to vaccinate against tuberculosis by the oral administration of a culture of live bacilli called BCG (bacillus Calmette-Guerin). This organism is of bovine origin and has been attenuated so that it has lost its tuberculogenic properties but retains its antigenic powers. It finds its greatest usefulness in newly born infants; the protection is prolonged to more than a year and can be repeated. In France, the mortality from tuberculosis in the first year of life has been reduced from 25 to 2 per cent without a single accident, febrile reactions or other unfavorable physiologic effects.

TREATMENT OF TUBERCULOSIS WITH SANOCRYSIN. BERNARDO BAMBACH and RAMON POMAR, Arch. Chilenos de Pediat. **3**:365, 1926.

The authors are unable to draw any conclusions from their examination of the literature on this subject, because of the great divergence of opinion on the efficacy of the drug. In large doses, sanocrysin is dangerous and produces violent reactions. The dose should not exceed 0.2 Gm. per kilogram of body weight. In the five patients treated, the authors have observed the toxic manifestations described by Mollgaard and his collaborators in Copenhagen.

DWYER, Kansas City.

EXAMINATION OF THE SPINAL FLUID IN SYPHILITIC CHILDREN AND ITS SIGNIFICANCE IN DIAGNOSIS, PROGNOSIS AND THERAPY. F. VON GUTFELD and S. MEYER, Arch. f. Kinderh. **75**:302 (March) 1925; **76**:13 (April) 1925.

Lumbar puncture was performed on 155 children who had a positive Wassermann reaction. The ages ranged from a few months to 16 years, and all but two had congenital syphilis. In only seventy-five children, however, was the spinal puncture made before beginning treatment. Twelve children gave strongly positive reactions and three weakly positive reactions. Symptoms referable to involvement of the central nervous system occurred more frequently in children having positive Wassermann reactions with the spinal fluid, but occurred at times even in those with negative reactions. Children with positive Wassermann reactions with the spinal fluid always had positive blood reactions, and the colloidal gold test was in entire accord with the Wassermann reaction. The reaction in the spinal fluid became negative long before the symptoms in the central nervous system disappeared.

T. C. HEMPELMANN, St. Louis.

THE FREQUENCY OF TUBERCULOSIS. F. HAMBURGER and J. MAYRHOFER-GRÜMBUHEL, Beitr. z. Klin. d. Tuberk. **63**:778, 1926.

This is a critical survey of the literature on the question. The authors arrive at the following conclusions: 1. A tuberculous infection can be excluded in children if they do not react to 1 mg. of old tuberculin; in adults 100 mg. is necessary. 2. In autopsy work reliable results are obtained only if microscopic studies and animal inoculations complete the macroscopic observations. 3. In order to arrive at a fair representation of the frequency of tuberculosis in the general population, it is necessary to base statistics not on hospital material and to exclude from autopsy records cases of lethal tuberculosis. 4. If such critical methods are used it is found that practically the entire population of civilized countries is infected at the age of from 20 to 25 years.

In large cities this complete infection is already accomplished at the age of puberty in the lower social stratum. In smaller towns, in the country and in well-to-do social circles, the infection becomes complete only at a later date. 5. In children the curve of frequency of infection increases evenly with increasing age.

MAX PINNER.

EPITUBERCULOUS INFILTRATION. W. KÖLZER, Jahrb. f. Kinderh. **115**:194 (Feb.) 1927.

There are two forms of epituberculous infiltration. The most common is found with active pulmonary tuberculosis. This is mostly localized; regression is possible, so that only the tuberculous areas leave residuals. The second type is the infiltration of Eliasberg and Neuland found in occult pulmonary tuberculosis. It usually involves an entire lobe or more. The upper lobe is most commonly affected. The tuberculosis is found in the hilum glands or elsewhere. This infiltration may disappear completely, but it is rare. The symptoms in both forms are the same. The recovery from epituberculous infiltration does not assure a local immunity against recurrence. There is no increased sensitivity to tuberculin.

PETERMAN, Milwaukee.

CONGENITAL SYPHILIS AND ITS SIGNIFICANCE FOR THE CHILD. S. A. GAMMELTOFT, Monatschr. f. Geburtsh. u. Gynäk. **75**:400 (Jan.) 1927.

All cases of congenital syphilis are considered maternal infections, the usual time for infection being the fourth or fifth month. The fetus is rarely infected during labor. Ninety-seven per cent of the offsprings of untreated syphilitic mothers were infected. Contrary to Kassowitz's rule, the probability of fetal infection does not always decrease in subsequent pregnancies.

Gammeltoft gives antisyphilitic treatment to all pregnant women with a syphilitic history, irrespective of the serologic examination. However, the general prophylactic treatment of the offspring is described. He thinks it unjust to label all these children as syphilitic. When the mother receives proper treatment, 80 per cent of the offspring are healthy, as judged clinically and serologically. Even if the infant has a weakly positive Wassermann reaction without clinical signs of syphilis, treatment is not given. If the infant has a negative Wassermann reaction, but the mother's Wassermann reaction is positive, treatment is not given. These untreated infants are kept under observation at least six months. If possible, infants are breast-fed unless the mother was infected late in pregnancy and delivered an apparently healthy infant.

BRAHDY, New York.

## Internal Diseases

GIANT CELL TUMORS NOT CONNECTED WITH BONES. L. D. CAMPBELL, California and West. Med. **25**:212, 1926.

The tumors are benign, affect both sexes equally, occur most often between the ages of 10 and 20 years, are preceded by trauma or inflammation about one third of the time and are treated successfully by excision. Macroscopically, they are encapsulated, lobulated, gray to yellow-pink nodules, at times mottled with brown, hemispherical and rarely as large as an egg. Microscopically, the dense fibrous capsule and trabeculae are infiltrated with tumor cells, contain pigment deposits and in places are hyalinized. The giant cells are from 9 to 100 microns

in diameter and contain from two to one hundred nuclei placed centrally. About one half of the tumors contain xanthoma cells with distinct cell membranes, small dark nuclei and a pale cholesterin containing cytoplasm. Blood vessels are abundant and often show signs of endothelial proliferation. Degenerative changes are constant and usually consist of cholesterin and hemosiderin deposits.

Campbell cites three new cases. The first two occurred on the tendons of the ring and index fingers of two women, aged 60. The third occurred in a man, aged 40, and apparently had its origin in the laryngeal cartilages.

GEORGE RUKSTINAT.

MEDICAL TREATMENT OF CHRONIC NONSPECIFIC INFECTIONS OF LUNGS AND BRONCHI OF CHILDREN. JOSEPH BRENNEMANN, J. A. M. A. **87**:801 (Sept. 11) 1926.

The three most important general measures in the medical treatment of these chronic nonspecific infections of the lungs and bronchi in children are rest, hygiene and nutrition. Drug therapy follows as a weak fourth. The greatest of all indications is rest in bed, for the child that is tired and weak belongs in bed. Partial rest in bed will not give results. Proper hygiene is the second indication. The child is better off in a warm, equable, sunshiny climate in a nonpopulous locality. If this is impossible the conditions must be met as nearly as possible at home, with such adjuncts as fireplaces, electric heaters, ultraviolet ray therapy and cod liver oil. The problem of nutrition is an important one and is intimately interwoven with other indications. It is commonly not so much a question of good food as of conditions that will make the child eat. A judiciously feigned indifference to whether he eats or not is commonly far more effective than coaxing or forcing, especially when combined with a strange environment and the absence of the mother. The nature of the food is hardly as important as the quantity. If the child will only eat a fairly well balanced diet and plenty of it, the food elements, the calories and the vitamins are unimportant. If the child likes milk and a quart a day will not interfere with his appetite and comfort, there is, of course, no objection to it. But if he will eat more if he drinks less, so much the better, and the physician should not worry over xeropthalmia or beriberi or any other less tangible evidence of vitamin deficiency. The question of medicinal treatment in these chronic infections is interesting perhaps more from a negative than from a positive standpoint. In painful, distressing coughs, opium in dosages sufficient to give relief is indicated. Steam inhalations impregnated with some soothing substance like compound tincture of benzoin and oil of eucalyptus would seem rational. Vaccine therapy in the cure of these conditions would seem to be justifiably restricted to an ever narrowing field.

MECKEL'S DIVERTICULUM AS A CAUSE OF INTESTINAL HEMORRHAGE. ISAAC A. ABT and ALFRED A. STRAUSS, J. A. M. A. **87**:991 (Sept. 25) 1926.

Three cases are reported of severe repeated intestinal hemorrhages, occurring in children aged 1, 2 years, and 2 years and 11 months, respectively, in which a fairly large Meckel's diverticulum was found responsible for the hemorrhage. Surgical removal of the diverticulum was followed by complete recovery of the patient in each instance. In two of the specimens ulcerations were found in the mucosa of the diverticulum. Persistent or occasional loss of blood occurred for about two months in all three cases, during which period

a high degree of anemia developed. It is the tendency toward repetition of the hemorrhage, which may be profuse at times, that is characteristic. Perforation occurred in none of these cases, but it is a frequent complication.

USE OF STANDARD DIET FORMULAS IN CONTROL OF JUVENILE DIABETES MELLITUS. J. S. BOYD, J. A. M. A. **87**:1070 (Sept. 25) 1926.

Because of difficulty in prescribing individual diets for children, basic diet formulas have been devised, which eliminate the necessity for calculation and insure a completeness of the diet, at the same time allowing sufficient variety to satisfy the appetite and to conform to seasonal changes in food supply.

THE PLASMA PROTEIN IN POSTURAL ALBUMINURIA. FREDERICK W. SCHLUTZ and W. W. SWANSON, J. A. M. A. **87**:1193 (Oct. 9) 1926.

The authors studied the blood plasma protein and the amino-acid concentration of both blood and urine of five children showing postural albuminuria. The plasma proteins were within normal limits. The constant drainage of albumin through the kidney capillaries is not sufficient to show a quantitative reduction in the plasma albumin, and there is no evidence that globulin is increased, as happens in many acute and chronic conditions in which the globulin appears to increase and compensate for loss of albumin. A study of the distribution of the amino-acids in the blood and urine revealed nothing abnormal. The concentrations found were well within the normal blood values and the value found in the normal urine. It is evident that the amino-acid concentration is not affected by change in the posture, or by the physical state of the subject.

CAN THE PROGNOSIS OF INFANTILE ANEMIAS BE BASED ON THE BLOOD PICTURE? A. A. ABALLI, J. A. M. A. **87**:2049 (Dec. 18) 1926.

The author believes that at present too much importance, from the standpoint of diagnosis and prognosis, is given to the morphology of the blood, leading to judgments that constitute an error of modern medicine, which, on returning to the strict anatomopathologic conception, loses sight of physiopathology. One of the great difficulties today is the tendency on the part of each author to create his own nomenclature in connection with the normal and pathologic elements of the blood. The errors resulting from basing all conclusions on simple data arising from corpuscular, leukocytic and differential blood counts constitute a substantial mistake, so far not sufficiently criticized, the necessity of referring these data to the total volume of the blood or at least of making a comparative valuation of the plasma and the formed elements not having been yet sufficiently generalized. From the study of the state of the blood in conditions of dehydration, physicians are aware of the errors that can arise from the sole consideration of blood elements. In the light of present knowledge, it becomes necessary today to study the etiologic factor of any blood disease, making use of all means that the laboratory can furnish in examination of patients, and thus arrive at proper and practical therapeutic deductions.

END-RESULTS IN THE TREATMENT OF DIABETES MELLITUS IN CHILDREN. ELLIOT P. JOSLIN, J. A. M. A. **88**:28 (Jan. 1) 1927.

In a special article by Dr. Joslin, the results of the treatment of 395 diabetic children during the last twenty-eight years were given. More than half are known to be alive. The duration of eight cases, in which three of the patients

are now dead and five are living, has exceeded ten years. The duration of the fifty-one fatal cases in the Naunyn epoch was 2.1 years; of the 110 fatal cases in the Allen epoch was 2.4 years, and of the thirty-four fatal cases thus far in the Banting epoch, 2.6 years. The duration of disease in fifty-two children now living, first treated in the Allen epoch, is 6.6 years. Pathologic and clinical evidence justifies hope for the future of the diabetic child.

BONAR, Salt Lake City.

THE EVOLUTION OF THE HEART AND ITS RELATION TO THE CARDIOLOGY OF CHILDHOOD. J. EPSTEIN, M. Clin. N. Amer. **10**:1063 (Jan.) 1927.

Confusion and mistakes are certain to occur if the heart of the child is regarded only as a smaller adult organ, endowed with the same anatomic, physiologic and pathologic characteristics. Correct evaluation of clinical signs and symptoms referable to the heart in childhood rests on a clear understanding of its recent rapid evolution from a primitive circulatory organ to a complete four chambered heart, and of the changes that it has undergone in adapting itself to extra-uterine life and later to the needs of the growing child. Physiologic disturbances of rhythmicity, irritability, conductivity, contractility and tonicity are common. Due to the fact that in the early stages of its development the heart is essentially a myogenic mechanism and only gradually comes under control of the nervous system, such phenomena as unsteady rhythm, sinus arrhythmia, extrasystoles, irregular and wavy contractions and reduplication frequently occur.

Murmurs may be physiologically or pathologically congenital, and physiologically or pathologically acquired. Physiologically congenital murmurs occur in the presence of patent ductus arteriosis and open foramen ovale; all other congenital murmurs are pathologic. Physiologically acquired murmurs include the so-called functional or accidental murmurs and are probably due to diminished tonicity. Pathologically acquired murmurs occur as the result of endocarditis or valvulitis.

The author urges a closer study of the fetal and infantile heart, since a clear understanding of the developmental peculiarities of this organ are necessary to a proper interpretation of clinical signs of circulatory disturbances in the young.

SMITH, Ogden, Utah.

TISSUE FIBRINOGEN BY MOUTH IN THE TREATMENT OF ACUTE HEMORRHAGE IN HEMOPHILIA. LLOYD B. DICKEY, M. J. & Rec. **124**:543 (Nov. 3) 1926.

The author reports two cases of severe hemorrhage. Case 1 was in an infant of 1 year of age, and bleeding commenced immediately after circumcision. Case 2 was in a boy aged 12 years, suffering from hemorrhage into the knee and elbow joints. In both cases tissue fibrinogen given by mouth in ice water on an empty stomach exerted a decided effect on the bleeding coincident with a marked reduction in the coagulation time of the blood. As the bleeding in hemophilia is difficult to control by other methods, the use of tissue fibrinogen by mouth deserves a further trial.

WILLIAMSON, New Orleans.

INFECTION OF THE RESPIRATORY TRACT IN THE INFANT AND CHILD. W. W. WASSON, Texas State J. Med. **22**:623, 1927.

The author makes a roentgen-ray study of the respiratory tract from birth through life. He includes the pharynx and the nose, with the accessory sinuses, tonsils and adenoids. The roentgenogram of the infant can be as accurate in

the portrayal of its structure as in the adult. The roentgenographic examinations reveal the normal structure and its physiologic and pathologic variations.

Faulty technic and lack of familiarity with the anatomy has caused much confusion. The shadows of the linear markings are cast by the arteries and bronchi. The accessory nasal sinuses develop from little sinuses the size of a pea and gradually enlarge to full sized sinuses.

In the first few months of life the frontal sinuses are absent and the antra, ethmoids and sphenoids, starting with tiny shadows the size of a pea, gradually enlarge, become prominent and readily distinguishable. Later, the ethmoids in their growth form the frontal sinuses, and so on, until the picture is complete.

Following these studies in development, any particular sinus may not remain clear, but evidence of infection will be seen. Sometimes it is only one antrum; later the infection spreads until all the sinuses are involved. Involvement of the sinuses occurs as early as 7 months, and in a year or fifteen months such infections are fairly common.

It is observed that associated with this involvement of the sinuses there is evidence of a bronchitis or even bronchiectasis. Wasson has found patients with asthma under 2 years of age with all the sinuses badly involved, and definite infection of the glands of the hila and the adjacent lung. Such conditions can hardly be diagnosed except by the roentgenogram. It is not necessary to anesthetize infants for these pictures.

Infected tonsils and adenoids may give a similar picture at the roots of the lung as infected sinuses. Treatment of the tonsils may or may not relieve infected sinuses, and likewise infected sinuses may contribute greatly to infections of the pharynx.

In any study of the lungs, one must consider: first, the lungs are the only internal organs connected with the outside air; second, all of the blood of the body must pass through the lungs; third, the lymphatics of the lungs are connected above with the lymphatics of the head and neck and below with the abdomen. These factors contribute a wider variety of disease to the lungs than to any other organ of the body.

In roentgenographic studies it is possible to divide the diseases of the lungs in children into three great classes: First, circulatory disturbances; second, tumors, and third, infections. In the disturbances of circulation, there is usually a large heart and congestion of the bases of the lungs. In tumors there is either a primary growth originating in one of the thoracic viscera, or secondary metastasis of tumors as carried to the lungs by the lymph or blood.

Infections of the lungs are subdivided into those involving the hila, the bronchi, the parenchyma or the pleura. Tuberculosis occasionally involves almost entirely the glands of either hilum, but in these cases the sinuses and tonsils are not contributing any part and would be a cardinal point in differential diagnosis.

In bronchitis there is the congestion, or fibrous changes of the bronchi, radiating out from the hilum on each side, while bronchiectasis involves chiefly the bases and has dilatations of the bronchi, the roengenogram giving a typical picture in differentiating the two conditions. LESLIE MOORE, Dallas, Texas.

BONE CHANGES IN RENAL AND CELIAC INFANTILISM. LEONARD PARSONS, Arch. Dis. Childhood **2**:1 (Feb.) 1927.

Parsons presents an excellent résumé of renal infantilism with a report of five cases. The roentgenographic manifestations were classified in three

groups: Atrophic-fragile, atrophic, osteoporotic appearance; florid—characteristic of florid rachitis; honeycomb—swollen epiphysis with woolly or stippled appearance.

The blood chemistry showed in many instances an extreme lipemia, in all cases a high degree of nitrogen retention (blood urea from 113 to 720 mg.); the non-protein nitrogen and creatinine were high. The serum phosphorus was greatly increased and the calcium low or normal. Evidence of the rachitic nature of the disease is based mainly on the roentgenologic examinations. The epiphyseal line is indistinguishable from true rachitis. One case came to autopsy. The histologic examination of the sections from the costochondral junction and from the lower epiphysis of the radius revealed a broad, irregular line of ossification with little calcification in the matrix of the cartilage. The columns of cartilage cells were distorted and broken up by irregular masses of vascular osteoid tissue. The bone deformities were considered those of true low-calcium rachitis with their origin in the inability of the kidney to excrete phosphate properly. The blood calcium is maintained at a higher figure than is usual in severe nephritis with phosphate retention by the mobilization of calcium from the bones; this is another factor in producing rachitis. Healing of rachitis may occur in those periods in which excretion of phosphorus improves materially or when the period of growth is over. Treatment of renal rachitis by ultraviolet radiation is contraindicated, since it aggravates the changes in the bones.

CHOLEMIA. J. C. SPENCE and A. G. OGILVIE, Arch. Dis. Childhood **2**:41 (Feb.) 1927.

The nervous symptoms associated with diseases of the liver are extremely interesting, particularly since Wilson's report of cirrhosis associated with progressive degeneration of the lenticular nucleus. Twenty-one cases of atrophy of the liver that came to autopsy are reported. Five of these were in children under 15. One case was acute and twenty were of subacute yellow atrophy. In all five children and in eleven of the adults, a certain sequence of nervous symptoms characterized the terminal or cholemic stage. This consisted of lethargy or stupor, a period of unusual shrieking and crying, a stage of convulsions, and death in coma. The most characteristic nervous symptom was the maniacal shrieking and wailing—termed "cholemic crying." Jaundice was present in all cases but varied greatly in degree, and bore no relation to the cholemic symptoms.

M. G. PETERMAN, Milwaukee.

CIRRHOSIS OF LIVER; TELANGIECTASIS; DEFORMITY OF METACARPAL. C. F. T. EAST, Proc. Roy. Soc. Med., November, 1926, vol. 20.

In a girl of 11 years, telangiectasis appeared on the face first at 18 months. In October, 1920, the liver and spleen were large and hard. The Wassermann reaction was negative. At the ages of 5 and 6, she had suffered from an attack of hematemesis and melena and had another attack of the former at 9 years. She was admitted to the hospital in 1926, suffering from diarrhea. In February, the Wassermann reaction was doubtful but positive in May. The liver and spleen were large and hard. The fourth metacarpal of each hand was abnormally shortened, which was due to a premature union of the epiphysis and body.

CASE FOR DIAGNOSIS (CONGENITAL HEART DISEASE). DOUGLAS FIRTH, Proc. Roy. Soc. Med., November, 1926, vol. 20.

A girl, aged 10 years, looked healthy and had neither dyspnea nor cyanosis; there was no clubbing of the fingers and no history of rheumatic fever. A soft systolic murmur and a diastolic murmurous noise were heard at the apex, in the recumbent position. A roentgenogram of the heart was normal: the electrocardiogram showed an inverted T-wave in leads II and III. While the child was in the hospital, diagnoses of congenital morbus cordis, organic mitral disease and an exocardial murmur were suggested. The case was shown to elicit opinions as to the murmur and as to whether the child should live a guarded life or a normal one.

WILLIAMSON, New Orleans.

DEFORMITY OF THE COSTAL CARTILAGES OF CHILDHOOD AND ADOLESCENCE. M. G. HUC, Paris méd. **8**:182 (Feb. 19) 1927.

The author observed at the Infants' Hospital modifications in the form, size and situation of the costal cartilages in children between 5 and 11 years. These consisted of two forms. The acute develops spontaneously in three or four hours and consists of a painful swelling that impedes respiration. These come at the junction of the sternum with the second, third and fourth cartilage. They are usually single and never bilateral. The skin is slightly reddened, and there is evidence of inflammation. The roentgenogram is negative. The author believes these to be caused by infection, as several healed under staphylococcus vaccine. However, one with a 3 plus Wassermann reaction healed under treatment with arsphenamine, and others cleared up spontaneously. The cartilages remain slightly enlarged and a little stiff.

The chronic form is usually discovered in the course of a routine examination, and consists of two forms. The first is a small tumor at the costochondral junction. The second is a depression made by a concavity in the cartilage. These are also believed to have been of infectious origin, the part becoming deformed due to lack of muscular action. The possibility of a latent rachitis must also be considered.

Treatment consists of gymnastics and breathing exercises. In infants, the best results are obtained by placing the child horizontally, and with a hand placed on the abdomen; the breathing then must become thoracic. The exercises are continued daily in increasing periods of time, and give beneficial results.

VACCINE THERAPY IN THE BRONCHOPNEUMONIAS OF INFANCY. L. DUCHON, Paris méd. **8**:188 (Feb. 19) 1927.

The author finds that bronchopneumonia is caused by seven groups of organisms: *B. influenzae*, streptococcus, pneumococcus, staphylococcus, *Micrococcus catarrhalis*, *B. coli* and *B. Diphtheriae*. The procedure is to make a culture from the nasopharynx and give the appropriate vaccines for the organism or organisms found. This is repeated after a period of apyrexia, and if any new organism is found, vaccination is also done for this.

Treatment consists of daily injections during the fever, which usually subsides by the fifth day, and two days thereafter. Another injection is given at the end of a week. The dose is 0.75 cc., which is increased to 1 cc. The mortality in 138 cases was 17.5 per cent.

SANFORD, Chicago.

THE PERCUSSION OF THE CRANIUM IN CHILDREN. R. STANKIEWICZ, Rev. franç de pediat. **2**:305, 1926.

Stimulated by the interest which has been shown from time to time in the percussion of the cranium, the author made a study of this phenomenon in 117 cases in which there was a question of the existence of increased intracranial pressure. The point chosen for the percussion, which should be of the direct type, was along the coronal suture between the frontal and parietal bossae. The observations were checked in every instance by lumbar puncture. As a result of his study, the author maintains that a tympanitic or cracked-pot note obtained by percussion over either or both sides of the cranium (Macewen's sign) is evidence of increased intracranial pressure, and as such may be of value in the early diagnosis of such conditions as hydrocephalus, meningitis, encephalitis and tumors of the brain.

LESLIE, Chicago.

KIDNEY FUNCTION IN THE VARIOUS DISEASES OF INFANCY. E. GABBAS, Clin. pediat. **8**:619 (Oct.) 1926.

The author studied the function of the kidney in twenty-seven patients suffering from various diseases. The many tests for nitrogenous retention were carried out, especially in comparison with Ambard's coefficient. When Ambard's coefficient is abnormally high, due to diminished kidney permeability, there is also a slowed and protracted elimination of creatinine. When the coefficient is subnormal, creatine elimination is accelerated. With a normal coefficient, the creatinine elimination is normal. Creatinine determinations offer a practical and helpful means of estimating kidney function.

ZAMBARANO, Northville, Mich.

A CASE OF CERVICAL RHEUMATISM WITH ENDOCARDITIS. EUGENIO CIENFUEGAS, Arch. Chilenos de pediat. **3**:233, 1926.

A boy, aged 20 months, became suddenly ill with high temperature, vomiting, diarrhea and great weakness. There was slight rigidity of the neck, petechiae of the abdomen and many bacilli and cocci in the urine. The condition was thought to be a colon bacillus septicemia, and injections of a sero-bacterin made from these organisms were given. A few days later, the condition becoming progressively worse, a cardiac murmur developed, with rapid loss of weight, and cardiac insufficiency was manifested by edema of the lower limbs, rapid, weak pulse, enlargement of the liver and dyspnea. Salicylates and digitalis were administered. The condition gradually improved, the neck rigidity disappeared, the weight increased and no perceptible sign of the endocarditis was present two and one-half months after the beginning of the illness.

A CASE OF ASTHMA IN AN INFANT. BAEZA GONI, Arch. Chilenos de pediat. **3**:235, 1926.

An infant, aged 14 months, living in a dark unsanitary room, became ill with bronchitis. The feeding had been breast milk exclusively for six months, then soup, pap and cow's milk. Rickets or latent tetany was not present. There soon developed signs of asthma, such as expiratory stridor, which became accentuated during sleep, with sibilant, stertorous râles in both lungs, and a normal temperature. The roentgenogram showed a hilum adenopathy and the Pirquet test was negative. The author does not believe this to be an

essential asthma in which the cause is not known, nor a manifestation of anaphylaxis. He classifies it as symptomatic asthma due to tracheobronchial adenopathy. Ultraviolet ray therapy is recommended, and it is suggested that the benefit from these rays is probably through their action on the visceral sympathetic nervous system.

DWYER, Kansas City, Mo.

INFANTILE ASTHMA. DR. SANTIAGO MUZZO PONS, Arch. Chilenos de Pediat. **3**:379, 1926.

The author studied thirty-five cases of asthma, and found that tuberculosis played an important rôle from an etiologic standpoint. It was definitely present in eleven cases. The other cases were attributed to a variety of causes, such as the exudative diathesis, florid rickets, thyroid and ovarian insufficiency, foreign body in the larynx and opium intoxication.

The author concludes that essential asthma does not exist and that in every case the exact cause should be determined.

DWYER, Kansas City, Mo.

THE TREATMENT OF GOITER IN INFANCY. A. ECKSTEIN, Arch. f. Kinderh. **76**:7 (April) 1925.

In the Freiburg goiter district, although 86 per cent of the boys and 95 per cent of the girls are goitrous, this anomaly is relatively rare in infants. It is interesting to note, however, that the average weight of the thyroid gland at birth is 10.5 Gm. in Freiburg, 5.7 Gm. in Göttingen, and 4.7 Gm. in Berlin. Goiter in infancy often causes severe stridor and even fatal asphyxia. The conservative treatment with potassium iodide has been found much more successful than operative procedures, improvement being rapid and marked. The administration of iodine must be watched carefully, since death has followed its injudicious or prolonged use.

T. C. HEMPELMANN.

THE TREATMENT OF PYELOCYSTITIS OF CHILDREN WITH AUTOVACCINE. ZOLTAN VON BOKAY, Jahrb. f. Kinderh. **110**:40 (Sept.) 1925.

Seven cases of pyelocystitis were treated with autovaccine, and the author draws the following conclusions: 1. The treatment with autovaccine appears hopeful. The greatest period of observation was seven months. 2. The value of vaccine therapy depends in a great measure on the amount of attenuated but not too attenuated organisms injected. A result is only to be expected when the injections are followed by an intensive general reaction (fever, chills). The dose must be determined for each case empirically and then increased. 3. The results begin to appear in from eight to ten days. 4. Fever that occurs two, five or seven hours after injection is high but not dangerous. The local infiltrations are painful and last fairly long.

IS GOAT'S MILK ANEMIA A DISEASE ENTITY? GERHARDT OCKEL, Jahrb. f. Kinderh. **110**:62 (Sept.) 1925.

Ockel finds that in alimentary anemias and in anemias of premature infants there is a marked polychromasia as a sign of increased regenerative power of the bone marrow or an indirect index of the increased destruction of red blood cells.

In his three cases of goat's milk anemia, there was no polychromasia indicating a lack of regenerative power of the bone marrow. He admits, however, that his last case showed many nucleated red cells.

E. W. EHRMANN, Chicago.

STUDIES IN OXYURIASIS. THERAPEUTICS. O. HEUBNER, Jahrb. f. Kinderh. **114**:127, 1926.

The author suffered from oxyuriasis for nine years. In the first part of these studies, published in 1922, he stated that he could not find any definite cure for his ailment. About seven weeks after each supposed cure, a new crop of worms developed in the intestinal tract.

In the present paper, he publishes his experience with a combination of different laxatives among which dihydroxyphtalophenon is the most important; and with suppositories containing alumen acetate and bismuth subiodgallate. His conclusions are that both drugs are valuable and that he was completely cured by the suppositories.

PARMELEE, Chicago.

A CASE OF DIABETES IN A NURSLING TREATED WITH INSULIN. H. J. FREYSCHMIDT, Monatschr. f. Kinderh. **35**:121, 1927.

Freyschmidt reports a case of diabetes in a nursling, aged 3½ months, with a sugar excretion of 18 Gm. a day and with a blood sugar of 190 mg. The child weighed no more than at birth but under treatment with insulin in doses varying from five to ten units did fairly well for a time. One day, however, following a dose of two units, the child collapsed and died suddenly. The cause of death was not certain. Possibly the atrophic infant is especially susceptible to a low blood sugar.

UNSPECIFIC HEMOPTYSIS IN CHILDREN WITH FIBROUS BRONCHITIS. MARTA BERGER, Monatschr. f. Kinderh. **35**:145, 1927.

In two children, aged 3½ and 7 years, with pneumonia, pleural punctures were done for diagnostic purposes. Immediately following, there was a spasm of coughing followed by expectoration of blood and a gelatinous mass containing lung tissue. The hemorrhage was not repeated, and both children made good recoveries. The etiology of the condition is not clear.

GERSTLEY, Chicago.

DIABETES MELLITUS IN CHILDREN. WERNER GOTTSTEIN and ARTHUR BOHE, Ztschr. f. Kinderh. **41**:287, 1926.

The case of a boy, aged 9 years, who was in the hospital for three and one-half months under treatment for diabetes mellitus, is described. On a diet of from 40 to 50 Gm. of carbohydrate and 1 Gm. of protein per kilogram of body weight, he showed a positive sugar balance with from 20 to 40 units of insulin a day and gained 5 Kg. in three weeks. Suddenly he developed an unusual hypoglycemic complex, becoming suddenly speechless. He sat up laughing and then became unconscious with a slow pulse. When he was given grape sugar he revived, and in the course of the next two days lost 2.5 Kg., which would indicate that the binding of water under the influence of insulin is a loose one. His slow pulse continued for some days, together with a disturbed mental condition, but he improved and later was sugar free on from 70 to 90 Gm. of carbohydrate without insulin, a higher tolerance than he had had before.

There are three observations to be made in this case:

1. The clinical picture of hypoglycemia may vary a great deal from that described in animal experiments. The first symptom may be an acceleration of the pulse, or as in this case, a bradycardia, an occurrence which previously

has not been reported. This hypoglycemic complex occurred, as has been noted elsewhere, in the presence of a glycosuria. Staub likes his patients outside of the hospital to show a little sugar in the urine, as he thinks that then the complex is less liable to happen.

2. The appearance of sugar in the urine in the tolerance test is dependent on the amount of water given at the same time, because the maximum excretion of sugar and of water may not coincide. Moreover, the concentration of sugar in the tissues is dependent on the amount of water immediately available. In a growing child with diabetes, when variations in the water economy are great, time relations between water and sugar excretions have a special significance. The sugar tolerance test should be used not as a test of the utilization of carbohydrate but of its distribution, and when insulin is being used, a hormone which lowers the blood sugar and at the same time affects the water economy, judgment is especially difficult as to the amount of quickly utilized carbohydrate in the tissues.

3. Despite variations, there is a far-reaching parallelism between the amount of sugar in the blood and the amount in the urine, but the former is the finer indicator, and it must always be remembered that this statement holds true only in the daytime, as the author has never seen a diabetic child who would not pilfer food at night.

A consideration of the cases here reported gives some ground for hoping that the aglycosuria will continue, partly because of the reaction and partly because children who are helped to reach the age of puberty are enabled to take advantage of a further development of the pancreas, which, it is suspected, occurs at this time, and because the pancreas may be favorably influenced by the changed function of other glands of internal secretion.

BLOOD CHEMISTRY IN BRONCHOPNEUMONIA IN INFANTS. ERICH NASSAU and HERBERT POGORSCHELSKY, Ztschr. f. Kinderh. **41**:326, 1926.

In fatal bronchopneumonia, hours and days before the end there were the same changes in the blood; that is, there was found constantly a hyperalkaliemia and hypoglycemia with an occasional diminution of the blood calcium and a slight concentration of the serum. A further increase of clinically unfavorable symptoms corresponded to an increase in the blood changes. The favorable care of bronchopneumonia, on the other hand, even when the clinical pictures seemed severe, showed little change in the intermediate addition of the important organic and inorganic substances. The significance of these observations appears not to be of great importance, in default of searching and numerous experiments. There is a lack of experimental work on other diseases with high fever. The coincidence of an increase of potassium in the serum with a lowering of the calcium content and of the blood sugar speaks for a stimulation of the parasympathetic system, which is borne out apparently by clinical observation. Often in children in which the disease runs a severe course and ends fatally, a marked lymphocytosis before death and many phenomena in the heart and circulation are to be understood only by the assumption of the stimulation of the vagus nerve.

OSTITIS FIBROSA CYSTICA GENERALISATA IN CHILDHOOD. W. TOBLER, Ztschr. f. Kinderh. **41**:334, 1926.

A case is described of ostitis fibrosa cystica generalisata occurring in a boy from Montana. The only other case in a child is that of Haberer, which is similar. The boy under discussion is now 11 years old and has a condi-

tion that is characterized principally by the formation of multiple cysts in the skeleton. The first appearance of the disease was observed at the end of his fourth year, or about seven years ago. It began in the skull bones, and in the course of four years ten cysts could be detected. Four years after the first symptom, the pelvis and right femur were affected and six years after the onset foci in the scapula, ribs and left tibia were discovered, before the skeleton was examined by the roentgen ray; it is possible that the cysts were present long before they were found. In all there were more than twenty sharply defined unilocular or multilocular cysts found by the roentgen ray. The development of the cysts was presumably never accompanied by pains or any noteworthy influence on the general condition, except in the case of the right femur, following a great strain on the focus and a resultant fracture. Pain and disturbance of function did occur. The cysts varied in size from that of a pea to that of an egg, and all of them remained confined to the bones on which they first developed. In the long bones the metaphysis was chiefly involved. The contents of the cysts were sterile and often consisted of a yellow or brown creamy substance, but more often this was of a serous nature, which microscopically showed principally polymorphonuclear cells. Giant cells could be demonstrated only in one observation. Histologically, the wall of the cyst was composed of fibrous cartilage and connective tissue and toward the center of the cyst, of granulated tissue; it was infiltrated with lymphocytes, plasma cells and a few leukocytes. In the granulated tissue polymorphonuclear giant cells could be seen. In the preparation examined, signs of bone deterioration were not found anywhere.

Since the first description of this disease by Von Recklinghausen, who emphatically declared that the fibrous transformation of the marrow was characteristic, all observers recognize this standard as important, but it has not been characteristic. On the contrary, the tissue has varied considerably. Many workers have not described the condition accurately and have omitted the mention of other components of the tissue, such as the redness and character of the cells and the blood supply, and these will vary in the same preparation. Von Recklinghausen required for the diagnosis the presence of giant cells, which in the case described by Haberer were so numerous as to give the appearance of a giant-cell sarcoma. But these cells vary in number and may be completely absent, and the presence of the cells depends on the stage at which the cyst is examined. Even the appearance of increased bone building and bone destruction, thought at first to be characteristic, will not be present when the disease has come to a standstill.

The histologic picture, then, varies a great deal. A tissue which at one time shows the appearance of a giant cell sarcoma may later be transferred to that of a solid fibrous tumor infiltrated with bone structure. This is of importance because these tumors may be removed under the mistaken diagnosis of sarcoma, and it is known that ostitis fibrosa is not malignant. The microscopic diagnosis is only one link in the chain, and the choice of a specimen removed for examination sometimes seems to be a matter of luck. Microscopic examination, however, in connection with the roentgen-ray and clinical observations, and with consideration of the many-sided histologic picture, speak for the diagnosis.

EMERSON, Boston.

THE OCCURRENCE OF FATTY LIVER IN FAMILIES. A. BJÖRUM, Acta Paediat. **6**:225, 1926.

Four children in the same family were found at autopsy to have enormous fatty livers. During life they had suffered only from gastro-intestinal dis-

turbances. The only other lesions found were catarrhal enteritis and, in three of the four cases, moderately severe chronic nephritis. HOLT, Baltimore.

INFLUENCE OF BISMUTH ON BLOOD FORMING AND WEIGHT OF ANEMIC CHILDREN. E. TUDOS and P. KISS, Orvosi hetil. **71**:142, 1927.

Bismuth had a stimulating effect on hematopoiesis and hemoglobin concentration in animal experiments. It is also well known that bismuth has a general good effect when used in the treatment of congenital syphilis. The authors have injected bismuth intramuscularly in doses ranging from 15 to 70 mg. in anemic, undernourished children. After from six to twelve injections given twice a week, increase of weight and increase of the hemoglobulin was found in nearly all of the cases. They recommend the use of bismuth as a stimulant of the hematopoietic system. ZENTAY, St. Louis.

## Nervous Diseases

A CASE OF AMAUROTIC FAMILY IDIOCY, LATE INFANTILE TYPE (BIELSCHOWSKY) WITH CLINICAL PICTURE OF DECEREBRATE RIGIDITY. GEORGE B. HASSIN, Arch. Neurol. & Psychiat. **16**:708, 1926.

The author found typical changes of amaurotic idiocy including diffuse vacuolation of the ganglion cells containing amorphous deposits, rarefaction of medullary nerve fibers, atrophy of all cerebellar layers and marked degeneration of the deeper layers of the occipital lobe and of the ganglion cells of the nucleus ruber. There was a lipoid accumulation in the adventitial spaces of the blood vessels.

THE CIRCULATION OF THE CEREBROSPINAL FLUID FROM THE STANDPOINT OF INTRAVENTRICULAR AND INTRASPINAL THERAPY. C. C. REQUIER and A. FERRARO, J. Nerv. & Ment. Dis. **64**:561, 1926.

The authors review the present theories as to the origin and circulation of the spinal fluid and present a large bibliography. They conclude that the fluid is carried from the ventricles to the subarachnoid spaces through the foramina of Luschka and Magendie, and also through the cerebral parenchyma. They believe that intraspinal therapy is of value because drugs penetrate the spinal parenchyma from the subarachnoid space and also are carried by an ascending current to the cerebral parenchyma.

ROY GRINKER.

CISTERN PUNCTURE IN CHILDREN. DONALD STEWART, Edinburgh M. J. **34**:36 (Jan.) 1927.

The author reports a series of 127 punctures in thirty-three children from 7 months to 12 years of age, eighteen of whom were suffering from meningitis. The technic is illustrated by diagram and photograph. The indications and the objections to this method are discussed. It is an easy and safe way of tapping the cerebrospinal reservoir, and an anesthetic is usually not necessary. It should not be used in advanced or moribund cases, or when puncture might injure vital tissues that have been displaced by disease. In cerebral tumor or other diseases in which the cistern is occluded, the method is contraindicated. For the treatment of acute meningitis by drainage, irrigation or serum, for diagnosis, and when lumbar puncture is not possible, the method is indicated.

NEFF, Kansas City.

A Child Recovering from Aphasia and Right-Sided Hemiplegia: Attacks of Jacksonian Epilepsy on the Right Side. F. Parkes Weber, Proc. Roy. Soc. Med., December, 1926, vol. 20.

A boy, aged 4½ years, was admitted to the hospital, March 17, 1926, suffering with complete aphasia together with slight spastic paralysis in the right upper extremity. No facial paralysis was present. The eye grounds and urine were normal. The boy was apparently of normal intelligence. The history obtained from the mother showed that the patient had suffered from fever for four weeks, when he suddenly became unconscious and had short convulsive attacks on the right side.

The boy was seen again on July 14. Great progress had been made in learning to speak, but the mother had observed twitchings on the right side, lasting about two minutes, after which the boy seemed dazed. These convulsive attacks apparently resembled slight jacksonian epilepsy on the right side.

On October 14, the boy was seen again. He was still awkward with his right hand. He would often let his mother know when a fit was coming on by calling "Mum" or making a grunting sound.

Williamson, New Orleans.

Acute Meningitis in Nurslings Produced by the Pfeiffer Bacillus. Prefort, Arch. de méd. d. enf. **30**:137, 1927.

The rôle of the Pfeiffer bacillus in the etiology of acute suppurative meningitis of infants has been the subject of intensive study, particularly in the United States. Among 1,600 children under 3 years of age admitted to the Visca Hospital, Montevideo, Uruguay, from December, 1922, to September, 1926, Prefort reports twenty-six cases of suppurative meningitis. The pathogenic agent in these cases was found, in fifteen infants, to be the meningococcus; in seven cases, the Pfeiffer bacillus and in the remaining four invasions, the pneumococcus. In its clinical aspects, meningitis produced by the bacillus of Pfeiffer does not differ in any important feature from that caused by other organisms, such as the streptococcus and those noted in the foregoing.

The mortality is 100 per cent, the exhibition of antimeningococcic serum not affecting the course of the disease in the least degree.

The histories and autopsy reports in the author's seven cases are published in full.

Amesse, Denver.

The Reciprocal Action of Pain and Alimentary Reflexes in Children. A. B. Wolowik, Jahrb. f. Kinderh. **115**:185 (Feb.) 1927.

Eighteen children from 2 months to 10 years of age were tested with the galvanic current before and after nursing or feeding. In the older children (from 7 to 10 years), the correlation between the alimentary and pain centers was less complete than in younger children. During feeding, the threshold in infants was reduced from one to two times and in older children only 30 to 40 per cent. Feeding produces a strong excitation of the alimentary centers, which causes an inhibition of other centers, especially that of pain. This inhibition disappears after satiation. During sleep and after feeding, the threshold of pain reflex is diminished. The threshold varies from day to day in the same child.

Peterman, Milwaukee.

CLINICAL OBSERVATIONS ON VAGOTONIA. VLADIMIR MIKULOWSKI, Monatschr. f. Kinderh. **35**:303, 1927.

Mikulowski reports the case of a boy, aged 13, who during his second and third years, on account of war conditions, was fed only rye bread. For the last six years, he had been vomiting large amounts of fluid every few days. He showed all the symptoms of spasmophilia. In view of the positive electrical phenomena, the asthenic habitus, the dilated stomach, slow respiration, bradycardia, hypotension and great tendency to fatigue, he was put in the class of the vagotonic. Treatment with epinephrine caused an increase in blood pressure, an increased urine and a change in the chloride excretion, but did not influence the clinical symptoms greatly. The addition of thyroid in amounts representing 20 cg. of the fresh gland caused an immediate improvement not only in the asthenia and the vagotonia of the stomach, but even was followed by the disappearance of the casts in the urine. There is considerable theoretic discussion of the subject of vagotonia.

GERSTLEY, Chicago.

THE PATHOLOGIC ANATOMY OF THE CHRONIC FORM OF EPIDEMIC ENCEPHALITIS. L. OMOROKOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:421, 1926.

In the two reported cases, special damage at the subcortical ganglion was not observed nor were vascular changes or infiltration found. There was a severe ependymitis without glial proliferation. Certain inclusions in the ependymal cells resembled parasites. Ganglion cell changes were most severe in the cortex and about the ventricles, and were peculiar in that the nucleoli were vacuolized.

ROY GRINKER.

## Diseases of the Ear, Nose and Throat

THE INFLAMMATORY PROCESSES IN THE COURSE OF MASTOIDITIS. JOSEF BECK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **15**:256 (Nov.) 1926.

The author states that the inflammatory process extends principally along blood vessels, and therefore spreads especially along the marrow spaces, but also along the vessels in the haversian canals. Cell infiltration of the marrow spaces takes place, accompanied by edema and hemorrhage. The fat becomes fibrosed, so that it can be called an osteomyelitis fibrosa. The fibrosis may be converted into bone. Empyema of the cells usually occurs; it is not a necessary part of mastoiditis, but only a part of the picture. The author shows pictures in which the cells are empty, and which are without reaction while the bone elsewhere shows severe inflammatory changes. The process may be productive as well as destructive of bone.

The mastoids with partially inhibited cell formation, which have the largest marrow spaces, and, as shown by Witmaack, the thinnest layer of cells, have the least resistance to inflammation. The sclerotic mastoid has few marrow spaces, and therefore it has few vessels. It shows little reaction to inflammation. It does not often develop mastoiditis, but, on the other hand, infection may spread through such bone to the cranial contents without sufficient reaction to defend the organism against this spread. Even in well pneumatized mastoids, intracranial extension may occur without resorption of bone, and in such cases it is difficult to decide the proper time to operate.

LEWY, Chicago.

MASTOIDISMUS AND MASTOIDITIS. FISCHER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **15**:283 (Nov.) 1926.

The local mastoid symptom complex, during the first week of otitis media, should be diagnostically distinguished from that of suppurative mastoiditis, and this is best done by accepting the term mastoidismus (Alexander). Mastoidismus heals under conservative treatment, but is converted into a suppurative disease by operative intervention.

[ARCH. OTOLARYNG.]

INTRACRANIAL COMPLICATIONS COMBINED WITH OTOGENOUS SINUS THROMBOSIS DURING THE LAST TEN YEARS. TIBOR GERMÁN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **16**:580 (Nov. 8) 1926.

The fact that patients wait for days or weeks before seeking expert advice for this condition is the cause of the high mortality. In the St. Rochus hospital in Budapest, during the last ten years, a cure was obtained in 65 per cent of the acute cases and in 38.9 per cent of the chronic cases. The operative method of choice is the ligation of the internal jugular vein and exposure of the sinus transversus until the healthy portion is reached. A hard tampon is placed between the bone and the sinus. The diseased sinus is laid bare and evacuated, and the lateral wall of the sinus is removed radically. The most frequent complications are: (1) perisinus respectively extradural abscess, (2) intermeningeal and subdural abscess, (3) leptomeningitis and (4) abscess of the brain.

Seventy-seven cases of sinus thrombosis with a demonstrable thrombus in the sinus were observed during the last ten years (1916-1925). Other cases are not mentioned. Germán considers in his essay only cases in which one or more intracranial complications existed besides the sinus thrombosis.

*Cases of Sinus Thrombosis*

| | Cases | Per Cent |
|---|---|---|
| Cases without intracranial complications | 27 | 35 |
| Cases with intracranial complications | 50 | 65 |
| Only perisinus or extradural abscess | 27 | 54 |
| Only intrameningeal or subdural abscess | — | — |
| Only meningitis | — | — |
| Only abscess of the brain | 3 | 6 |
| Extradural abscess, subdural abscess | 1 | 2 |
| Extradural abscess, subdural cerebellar abscess | 1 | 2 |
| Extradural abscess, brain abscess | 7 | 14 |
| Extradural abscess, meningitis | 4 | 8 |
| Extradural abscess, abscess of the brain, meningitis | 2 | 4 |
| Subdural abscess, meningitis | 1 | 2 |
| Abscess of the brain, meningitis | 4 | 8 |

Of the seventy-seven patients, 27 or 35 per cent, did not show any intracranial complications. An extradural abscess was the only complication in 27, or 54 per cent, of the remaining fifty, or 65 per cent, of the series. These are not described. Only the histories and course of disease in the remaining twenty-three cases are given. A thorough critical review follows, which deals with the various complications, their development and their pathology. This must be read in the original. Incidentally, Germán mentions an extradural abscess following a cholesteatoma. The patient exhibited photophobia as the most pronounced sensory symptom. He was reluctant to open his eyes for weeks. Other symptoms of meningitis were absent. The patient recovered.

AMBERG, Detroit.

## Diseases of the Skin

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA. A. M. H. GRAY, Proc. Roy. Soc. Med. **20**:343 (Feb.) 1927.

A boy, aged 13, an inmate of an orphan institution, for seven months had developed spots on his body which formed small crusts, and these, on falling off, left pitted scars. The condition was thought to be varicella, but as the lesions continued to appear he was referred for diagnosis. The earliest lesions were pale pinkish yellow, slightly elevated papules with smooth nonscaly surfaces varying in size from that of a lentil to that of a pea. On rubbing they became brighter red, but wheals did not develop. They were discrete and did not tend to group. A large number soon developed a central hemorrhage and dried up, forming a dry scab, which after some days fell off and left a pitted scar. Some, however, did not necrose in the center but gradually faded away leaving a yellowish stain for a time. Occasionally, one found a flat, almost colorless lesion, covered with fine branny scales and greatly resembling the lesions seen in pityriasis lichenoides chronica (parapsoriasis en gouttes). Intradermic tuberculin tests were positive and roentgenograms revealed "Suspicious infiltrating shadows upper part of both lungs especially the right. Lower parts of both lungs are quite clear."

GUY, Pittsburgh.

A CASE OF ACUTE LICHEN PLANUS IN A CHILD. LORTAT-JACOB and ROBERT SICARD, Bull. Soc. franç. de dermat. et syph. **34**:26, 1927.

In a child, aged 8 years, the eruption was of abrupt onset, rapid evolution and generalized distribution. The buccal mucosa was not involved.

[ARCH. DERMAT. & SYPH.]

NASAL RESPIRATORY DIFFICULTIES IN THE NURSLINGS. ENRIQUE PRADA, Arch. español. de pediat. **11**:86, 1927.

More than 90 per cent of nasal respiratory difficulties in nurslings are due to acute coryza. The author believes that acute adenoiditis is exceedingly common. He advises against adenoidectomy in early infancy. He advocates the use of local treatment in the form of solutions containing hydrochloride of cocaine and epinephrine, and also the use of mild or strong silver protein solutions. He emphatically warns against all nasal irrigation.

SCHLUTZ, Minneapolis.

DERMATOSIS DUE TO ASCARIDIASIS, RESEMBLING HEBRA'S PRURIGO. A. CEDERBERG, Arch. f. Dermat. u. Syph. **150**:393, 1926.

The case of a boy, aged 8 years, physically retarded, with many ascaris eggs in the stool and the skin dry and pigmented in places, was diagnosed as Hebra's prurigo. From the age of 6 months to 5 years he had had a generalized, itching, pin-head sized, papular skin eruption which was then supplanted by a small papular rash most marked on the extensor surfaces but noticeable also on the flexor surfaces, abdomen and back. After the administration of santonin, fifty-seven ascarids were passed. The author concludes that ascari infection may lead to urticaria, an anaphylactic manifestation of an intoxication. At the height of the intoxication there were 15,500 lymphocytes per cubic millimeter, and the eosinophils constituted 47 per cent of the white cells. The hemoglobin was 70 per cent (Sahli) and the red cell count was between 3,500,000 and 4,000,000.

GEORGE RUKSTIUAT.

RESEARCHES ON APHTHAE (POPISCHILL). ALFRED FESSLER and FREIDRICH FEYRTER, Ztschr. f. Kinderh. **41**:489, 1926.

Popischill has described a disease of the skin and mucous membranes which he saw develop in cases of measles and pertussis. Thick walled vesicles appeared, the center of which fell and became dry and crusted. They occurred chiefly on the tongue but also on the lips, on the mucous membranes of the mouth, throat, larynx, esophagus and on the face. The picture is that of a disease of the skin and mucous membranes, with a cellular fibrinous exudate between the epithelium and the stroma underneath, as well as in the deep layers of the epithelium. In the skin it is accompanied by para and hyperkeratosis. There is simultaneously deep reaching localized cellular infiltration of the mucosa and the submucosa and of the cutis and subcutis, especially around the vessels and in the skin around the follicles.

Eight cases are here reported in children, from 3½ months to 3½ years old, which occurred secondary to fatal measles, pertussis, scarlet fever, diphtheria and possibly German measles. The tonsils were regularly spared, which is of diagnostic importance. It is interesting that the frequent localization of the process in the larynx may lead to huskiness and stenosis.

In two cases, scrapings were taken from the ulcers and transplanted to the scarified conjunctiva of rabbits; a sterile conjunctivitis resulted, but transplantation to the mucous membrane of the mouth was less successful. The rabbits did not develop immunity later. Attempts to connect aphthae (Popischill) and herpes febrillous faciei by crossed immunologic experiments were negative.

THE ETIOLOGY OF STILL'S DISEASE AND FOCAL SCLERODERMA. W. STOYE, Ztschr. f. Kinderh. **41**:538, 1926.

In a girl, aged 5, with Still's disease and many rheumatic nodules, Stoye watched the transformation of one of the nodules to a focus of scleroderma, which began in the subcutis and spread in all directions. Nonhemolytic streptococci were obtained from the blood at death, although repeated cultures during life were negative. Since rheumatic nodules are often found in Still's disease, the scleroderma was not an accidental complication but a local product of a specific disease, a chronic infection with streptococci of little virulence. It is related to chronic rheumatic infection in children but is not identical with it. The synovial membrane of the knee joint showed chronic inflammation, with hyperplasia of the joint capsule but without exudation into the joint space. A synovitis, then, contrary to the general impression, may belong to the picture of Still's disease.

EMERSON, Boston.

## Surgery and Orthopedics

SARCOMA OF THE PROSTATE IN AN INFANT OF NINE MONTHS. M. LAQUIÈRE and R. BOUCHARD, J. d'urol. Paris **22**:244, 1926.

An infant of 9 months presented the clinical signs of prostatic enlargement. At operation for the drainage of a supposed abscess, the prostate was found to be enlarged, hard and white. Biopsy confirmed the operative diagnosis of sarcoma. The infant died ten days after the operation. Autopsy showed the prostate to be completely invaded by sarcoma of the spindle cell type.

WALTER M. SIMPSON.

## Miscellaneous

ULTRAVIOLET THERAPY IN PEDIATRICS. EDWIN T. WYMAN, M. J. & Rec. **124**: 628 (Nov. 17) 1926.

Ultraviolet rays are now recognized as a valuable therapeutic measure in the treatment of many diseases of infancy and childhood. Direct sunlight is probably the most effective way of giving this form of treatment. The scheme of exposure is described at length in the paper.

The mercury vapor quartz lamp can be used as a substitute for sunlight and has the advantage of being available regardless of sunshine and weather. It can be used indoors, and the doses can be gaged accurately.

Ultraviolet therapy is a specific in the treatment of rickets and spasmophilia and is a valuable therapeutic agent in the treatment of tuberculosis of the mesenteric and bronchial glands and tuberculous peritonitis. It is also useful in psoriasis and some persistent skin infections. There is, however, a danger of becoming too enthusiastic about this therapy in case it should be looked on by the physician and his patient as a quick and sure cure for all ailments.

WILLIAMSON, New Orleans.

STANDARD MILK ORDINANCE RESULTS IN FOURTEEN ALABAMA TOWNS. LESLIE C. FRANK, S. W. WELCH and C. A. ABELE, Southern M. J. **20**:233, 1927.

As an experiment, the standard milk ordinance of the United States was put into effect in fourteen Alabama towns. There was marked improvement in the quality of the raw milk supplies. Based on percentage rating, there was 115 per cent improvement. The quality of raw milk delivered to pasteurization plants improved 97 per cent. The care with which the pasteurization process was carried out improved 286 per cent.

Five of the fourteen towns are now having more than 50 per cent of all raw milk pasteurized. The milk sanitation rating of the fourteen towns improved 142 per cent. The milk consumption in these communities has increased more than 90 per cent.

The foregoing figures are truly impressive and indicate the possibilities when an intelligent organized effort is made in a community to enforce and carry out the standard ordinances.

SCHLUTZ, Minneapolis.

POVERTY, NUTRITION AND GROWTH. STUDIES OF CHILD LIFE IN CITIES AND RURAL DISTRICTS OF SCOTLAND. Special Report Series No. 101, Medical Research Council, London, 1926.

This report covers an intensive study of child life in the cities and rural districts of Scotland. It includes a description of the population studied and the methods employed, a comparison of children of the poorer classes in town and country and factors generally considered as influencing the nutrition and growth of children, such as income, home conditions, diet and parental factors.

Briefly, the conclusions are as follows: This study must be considered a pioneer work, as the first extensive attempt to estimate the influence of various environmental conditions on the growth and nutrition of the child of the slums. Such work cannot be expected to yield results of definite finality, and like most other scientific investigations it raises more questions than it answers, points out lines for further work, and indicates the difficulties of such attempts to elucidate social conditions. It does, however, seem to show that heredity and the inherited

growth impulse play no small part in determining the growth of the child, and that in spite of environmental factors, which may appear prejudicial, the slum child tends to develop on the lines of its parents. The apparent lag in the growth of the town child as compared with the country child, before the middle of the second year of life, indicates that future investigations must concentrate on this period.

Of the environmental characters studied, "maternal efficiency" seems more closely associated with variations in the condition of the child than the measures of "poverty," "underfeeding" or "overcrowding." One cannot, indeed, on the present evidence determine the precise nature of the relationship and, hence, determine what hindering circumstances are to be overcome or what good is to be encouraged out of the complex of good and bad qualities that lead to an assessment of "maternal efficiency." But these studies suggest that "maternal efficiency" is not directly and immediately associated with "poverty," but is, at least to some extent, associated with size of family, cubic capacity of the house per person, i. e., with overcrowding and with maternal health. BUHRMAN, Chicago.

DEFICIENCY OF SUNLIGHT AND INFECTIONS. P. WORINGER, Rev. franç. de Pédiat. **2**:161 (June) 1926.

This statistical study of disease incidence reveals several types of curves. One type follows in a singularly exact manner that for spasmophilia. Among the infections showing this characteristic are pneumonia, meningococcic meningitis, tuberculous meningitis, epidemic encephalitis and streptococcic infections such as puerperal fever. Measles and scarlet fever are more variable, although among an adult population the greatest incidence is in the late winter and early spring. The author calls the causative agents of these infections photophobic, and believes that the action of the ultraviolet rays on the skin produces a substance that is antagonistic to these organisms. An individual deprived of the ultraviolet rays over a prolonged period, such as occurs during the winter months, loses his ability to combat these infections at their onset; hence the rapid increase in cases at the end of the winter months. Another type of curve shows the rise in August, September and October. This includes the typhoid and dysentery group and also poliomyelitis. These organisms he calls photophilic. Other diseases show independent curves. Whooping cough does not show any consistent seasonal variation. Diphtheria shows a rise in fall and winter. The practical suggestion that comes out of this study is the prophylactic use of the ultraviolet rays during the winter months. LESLIE, Chicago.

COORDINATION OF HEALTH MEASURES FOR INFANTS: ORGANIZATION OF NIPIOHYGIENIC AND NIPIOLOGICAL INSTITUTES. CACACE, Rev. internat. de l'enf. **2**:616, 1926.

In 1905, at Capua, and in 1915, at Naples, Professor Cacace succeeded in consolidating all the existing agencies dedicated to the promotion of infant welfare. These organizations are known as nipiohygienic institutes. They include, in addition to a welfare section, an educational department and a division of social advancement. The death rate in the infant wards of these societies has dropped to about 2.5 per cent, while the courses in hygiene have been completed by 1,700 students. The child is studied from various points of view — biologic, sociologic, psychologic, legal, etc.

PROTECTION OF NURSING MOTHERS IN FRANCE. ICHOK, Rev. internat. de l'enf. **3**:92, 1927.

In view of the disheartening increase in infant mortality among the industrial classes, as compared with those not gainfully employed, France enacted a law in 1917 providing for the protection of nursing mothers. The effect of this legislation may now be noted in the improved vital statistics of the great manufacturing centers, especially in the north, where every conceivable comfort is extended to mothers in the nursing care of their infants. Separate rooms, well heated and properly ventilated, are provided in buildings wholly detached from the work rooms, where the mothers may not only nurse the infants at regular intervals, but where they may also secure needed rest and refreshment. An attending physician is charged with supervisory powers and is expected to be particularly diligent in the prevention of communicable disease.

AMESSE, Denver.

THE DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF DEFLECTION OF THE BLOOD PICTURE TO THE LEFT. A. HOFMANN and A. WELCKER, Arch. f. Kinderh. **76**:1 (April) 1925.

Despite the fact that the infants in this study were normal in every respect, the leukocyte counts ranged from 6,200 to 21,100. The differential count was as follows: basophils, 0 to 2 per cent; eosinophils, 0 to 7 per cent; neutrophils, 5 to 55.5 per cent; lymphocytes, 42.5 to 90.5 per cent; mononuclears, 0 to 16 per cent, and Türk and plasma cells, 0 to 3 per cent.

FATE OF CHILDREN IN FOUNDLING INSTITUTES AND THE INFLUENCE OF LATER HOME CARE. M. ZWINGENBERGER, Arch. f. Kinderh. **76**:27 (April) 1925.

In the first year of life, the mortality among 278 children in the St. Augustine home was 22.63 per cent, whereas of 106 whose fate was ascertained after dismissal, nineteen (17.92 per cent) died. In the second year, the mortality in the "home" was 0.93 per cent and outside, 6.9 per cent. In another "home," the mortality was 4.44 per cent (among 135 infants) in the first year, but was 18.92 per cent for the thirty-seven infants outside the "home." In the second year, the mortality was 1.55 per cent in the "home" and 3.33 per cent outside.

T. C. HEMPELMANN.

DETERMINATION OF SEX BY MONOILOFF'S REACTION. G. ALTERBERG and A. HAKANSSON, Biochem. Ztschr. **176**:251, 1926.

In 1924 Monoiloff described a complicated chemical color reaction, making use of five different reagents, the outcome of which was believed to make it possible to detect the male or female origin of blood or any other material. This reaction was held to be of universal biologic application and to be capable of differentiating the origin of substances of plants as well as animal origin. This contention, if established, would make the reaction of the utmost forensic importance. The authors working at the University of Lund investigated the various factors which enter into the reaction and the outcome of the reaction itself. They found that the relative proportion of the extracted material to be tested was an important factor in the reaction, that specific enzyme activity did not play any part, and that the result obtained was due in part at least to reduction and oxidation reactions brought about by the materials used. They conclude that the reaction has only a quantitative and not a qualitative application, and that it has no forensic value in helping to determine the male or female origin of any suspect material.

O. T. SCHULTZ.

THE POSTURE OF INFANTS. A. PEIPER and H. ISBERT, Jahrb. f. Kinderh. **115**:142 (Feb.) 1927.

In the new-born infants, body posture is determined entirely by the reflexes. The tendency in development is toward the erect posture. This is the function of the cerebrum, which makes great development in the first year. A complicated reflex system assists in the acquisition of new static functions until it is controlled by the cerebrum. The following posture reflexes are present at birth: labyrinth position reflex for the head; neck position for the body, and body posture for the head. Later, the suspension reflexes appear. The latter determine the erect posture and relieve the cerebrum of this function. Another reflex system which may be attributed to evolution disappears in the first year. This includes the fright reaction, embracing reflex, sleep reflex, and the hand reflex. These reflexes are controlled by the cerebrum and gradually disappear. This explains why these reflexes persist in idiots in whom the development of the cerebrum is limited. The group of tonic throat reflexes are more obvious the younger the child. They are a deep evolution phenomenon and may be found in the fetus. The protective reflexes are the eye reflex, the throat and the spinal reflex, and the embracing and the hand reflexes.

PETERMAN, Milwaukee.

THE STATUS OF THE LUNG TEST. F. STRASSMAN, Monatschr. f. Geburtsch. f. Gynäk. **74**:47 (Nov.) 1926.

The lung test in which distension of the alveoli (floating) has been used as proof of the entrance of air into the lungs may be questioned. Cases have been cited in the literature in which distended lungs have been found in infants born dead. Two cases (fetuses) are reported in which the alveoli were distended with amniotic fluid. The microscopic sections looked as if the alveoli had been distended with air.

THE BACTERIOPHAGE THERAPY IN CHILDHOOD. WALTER POCKELS, Monatschr. f. Kinderh. **35**:229, 1927.

In a research on the bacteriophages of d'Herelles, the author did not find them of any value in ordinary pyurias and nutritional disease. In the therapy of staphylococcus infections, however, he got good results when he used a bacteriophage that had been shown specific in test tube experiments.

GERSTLEY, Chicago.

CONDITIONS AFFECTING ACTION OF DIURETIN. M. GROSSMANN, Wien. klin. Wchnschr. **40**:285 (March 3) 1927.

Grossmann repeated his previous clinical experiments which demonstrate, he believes, that diuretin administered by mouth acts as a diuretic only in persons with achlorhydria. In patients having normal or increased gastric acidity, the drug may have no effect but more often causes a decreased excretion of urine. His explanation is that the hydrochloric acid combines with diuretin to form an inert or antidiuretic compound. Pure theobromine and its isomer theocin are not affected by hydrochloric acid. They should therefore be used in place of diuretin, when the peroral route is selected.

OLMSTED, Seattle.

# Society Transactions

## CHICAGO PEDIATRIC SOCIETY

*Regular Meeting, Jan. 18, 1927*

GEORGE E. BAXTER, M.D., *presiding*

ORANGE JUICE AND EGG YOLK MIXTURES FOR INFANT FEEDING. DR. JULIUS H. HESS.

Previous experimental work (Hess, J. H.; Koch, Elizabeth M., and Sennewald, Zella C.: Peptic Digestion of Cow's Milk, J. A. M. A. **87**:17 [Oct. 23] 1926) prompted a clinical study of the value of adding orange juice and raw egg yolk to the milk mixture of artificially fed infants.

Experiments in vitro were run to determine the effect of peptic digestion on fresh, raw, pasteurized and boiled milk, cultured lactic acid milk and also on raw milk to which hydrochloric acid, U. S. P., lactic acid, phosphoric acid, lemon juice, orange juice, fresh and canned tomato juice, sodium citrate, sodium bicarbonate and lime water had been added. The results show that these various modifications affect the solubility of the milk proteins as well as the digestibility.

After a consideration of the results of in vitro experiments on peptic digestion and in the character of the curds obtained after feeding puppies the various milk modifications, orange juice was selected in preference to the other inorganic and organic acids because it introduces vitamins, carbohydrate and mineral constituents. Therefore, it seemed to be the logical choice for continued feeding as an addition to raw, pasteurized or boiled milks. Raw egg yolk is of value because of its high iron, fat-soluble vitamin and fat content.

Feeding experiments were carried out on normal artificially fed infants. Individual cases were selected from about 1,300 breast-fed and bottle-fed infants in attendance at three City Infant Welfare Stations and at the University of Illinois Educational and Research Hospital Dispensary. Of the seventy-four infants selected, twenty-eight were observed through a minimum of eleven weeks of experimental feeding, with an average of fifteen weeks. The infants were brought for observation each week; body measurements were taken at the beginning and end of the study, and also hemoglobin readings and photographs. The infants were placed on a feeding calculated in terms of their body weight. They were fed amounts approximating 2 ounces (59 cc.) of milk and $\frac{1}{10}$ ounce of cane sugar per pound of infant weight. Sufficient water was added to bring the total fluid up to from $2\frac{1}{2}$ to 3 ounces (74 to 89 cc.) a pound. The mixture was boiled in a single boiler for three minutes, and after cooling 1 ounce (30 cc.) of orange juice was added for each pint of milk in the mixture. At the same time raw egg yolk was added in amounts varying from $\frac{1}{8}$ to $\frac{1}{2}$ of a yolk. Cod liver oil, in amounts from 1 to 2 teaspoonfuls, was fed throughout the study. Seventy-five per cent of the infants were under 3 months of age when the feedings were started.

During the total period of 151 weeks, while orange juice and raw egg yolk were added to the mixture, the twenty-eight infants made an average gain of 6.46 ounces (184 Gm.) a week. The infants took kindly to the feedings. In no case was any reaction to egg yolk observed, although in private practice,

in approximately 400 infants fed on this mixture, about one in fifty gave evidence of being sensitive to the egg yolk proteins. Orange juice can be started as early as the second or third week of life. Occasionally, an infant who receives the full amount will show some increased flatulence and looseness of the bowels, especially when very sour oranges are used. In such cases the orange juice may be reduced to ½ ounce (15 cc.) to the pint of milk. Raw egg yolk may be fed to infants as early as the third or fourth week. Beginning with ⅛ of the yolk, the amount may be increased to the whole yolk by the third month. While the infants were fed on this mixture the stools became yellow and much more plastic than those of ordinary milk mixtures — resembling closely the stools of breast-fed infants.

DISCUSSION

DR. JOSEPH BRENNEMANN: I wish to congratulate Dr. Hess on his conclusion that the nature and size of the curd is one of the most, if not the most, important things in the whole question of infant feeding. I have not said anything about curds for a long while, but I believe now, as I always have, that the size of the curd is important. Every therapeutic food that I have ever used has a fine curd as a desideratum. I am glad that experimental work with puppies gave results similar to those obtained in man. I tried the experiment on the dog when I was working on the size of the curd but found nothing in the adult dog's stomach that resembled that of man. The curds Dr. Hess has shown that returned from the puppies correspond exactly with those that return from the human subject.

I am interested in the orange juice and egg yolk feeding. When Hess of New York first brought out such a combination, it seemed like a logical and simple way of adding an acid, an antiscorbutic and an antirachitic to the food. If egg yolk is a good substitute for cod liver oil, it would be a great boon to the mothers by keeping their babies from smelling of cod liver oil. I think cod liver oil is still the thing, but I have a feeling that something else soon will be used, probably some irradiated substance that has less disagreeable features. One of the manufacturers of dried milk is thinking of irradiating the product, but there has not been enough experimental work on this as yet. There are two things about which I should like to have Dr. Hess tell us his experience. I have never seen in print, except what I have written myself, the statement that orange juice makes some infants vomit. I have seen this frequently, many of them vomiting not only the orange juice but the next feeding. In some of these cases, I have for some time been putting the orange juice into the milk. This has a tendency to overcome the vomiting in some instances, but in others it apparently has not. To me this is a real factor, and I wish some one would find out why orange juice makes quite a few babies vomit. The other thing I should like to have Dr. Hess describe concerns the well-known, not infrequent allergic reaction to egg albumin. The first time I ever tried egg yolk as a substitute for cod liver oil, I put one drop of egg yolk in one feeding. About two hours later, the mother called me and said that the child was covered from head to foot with an intensely itching rash. That lasted twenty-four hours and the child has never been able to take egg since. I would be afraid to give ⅛ or ¼ of a yolk to begin with if one drop can do what it did in this case. I should like to know whether Dr. Hess has had any unpleasant experiences of this kind with the larger amounts he has used.

DR. GEORGE E. BAXTER: I should like to know whether Dr. Hess has had any experience with cooked and uncooked egg yolk.

DR. I. M. CHAMBERLAIN: In the work at the four stations, there have been sixty-seven infants selected as suitable for this particular experiment. When my associates and I first started it seemed simple to get all the artificially fed infants one wished, but we soon found that it was difficult to get normal artificially fed infants; we have been able to find only sixty-seven in three months. Of these sixty-seven infants, forty were carried through the experiment. These infants were all placed on orange juice milk, to which egg yolk was added. In no case in this series has there been any reaction to the egg yolk. In no instance did we find that the infant refused to take the orange juice mixtures.

As to the actual results of the experiment, I think we are ready to offer one fact; that is, our infants seem to thrive well on the mixture. The others report that they take it well and from our observations and weekly check-ups, physically and by weight, they seem to be doing satisfactorily. The hemoglobin curve in all infants carried through the experimental period has shown a material improvement.

DR. KING G. WOODWARD, Rockford, Ill.: In the children in the Rockford Children's Home, ranging in age from 1 month to 5, I changed all the feedings simultaneously to orange juice milk, with gratifying results. I did find in private practice, when there was difficulty in getting a good grade of oranges, that there was some trouble. The infants vomited occasionally, and there was considerable excoriation of the buttocks. By cutting down the amount of orange juice this was remedied and later, when a good grade of oranges could be obtained, not any ill effects were noticed.

DR. HESS: I am glad that Dr. Woodward spoke of his experience, and I was hoping that others would tell of their difficulties. Dr. Chamberlain told me about three months ago that a number of his infants whom he was feeding orange-juice-egg-yolk milk had suddenly developed diarrhea with an associated fever. He raised the question as to whether the orange juice or the egg yolk might not have been the cause. I had a similar experience about this time, and on inquiry among our friends we found that there was an epidemic of what has been called "intestinal flu" by many of the physicians for want of a better term. Following this acute illness, the same infants were kept on the orange-juice-egg-yolk mixture without further disturbances. I am inclined to believe that Dr. Woodward's experience could be grouped with our own. It is true that some of the infants developed colic when the full amount of 1 ounce (30 cc.) of orange juice to the pint of milk was used. This, however, disappeared when the amount of orange juice was reduced and did not recur when it was gradually increased. It is also true that eggs contain bacteria among which *Bacillus pullorum* is a common invader. This organism may gain entrance to the egg while in the oviduct. It is also well known that bacteria may get into an egg through the shell. Of all foods, so far as is known, eggs are less liable to convey disease or to contain harmful properties than any other single food of animal origin. The literature is singularly free of instances of sickness attributable to eggs. In the diet of infants, only eggs of good quality should be considered as proper food. I have fed about 400 infants in my own practice on the orange-juice-egg-yolk mixture and have come to the conclusion that, on an average, not more than one infant in fifty becomes acutely ill from the egg yolk in the diet. Approximately one eighth of an

average yolk is added to the infant's diet by the time it is 1 month old, and this is increased to a whole yolk at the beginning of the fourth month.

With reference to sour oranges, I have had no bad experiences. They are certainly less acid than the average lemon, the juice of which has been recommended by Alfred Hess as an addition to milk mixtures. I have used the lemon juice milk successfully. The citrates are a factor in holding the protein in suspension. As to the addition of sodium citrate in amounts of 2 grains (0.13 Gm.) to the ounce of milk, it prevented the formation of curds for a period of at least from one-half to one hour after the milk had entered the stomach. For several years, the addition of sodium citrate in amounts of 2 grains to the ounce of milk was common practice in prescribing feeding for infants. I feel certain that I saw more cases of rickets in private practice then than I see now and that they were of a more severe grade.

PREMATURE INFANTS: A REPORT OF TWO HUNDRED AND SIXTY-SIX CASES. DRS. JULIUS H. HESS and I. M. CHAMBERLAIN.

The special station for premature infants at the Sarah Morris Hospital for Children of the Michael Reese Hospital has a capacity for the care of twenty infants. There are three rooms, one of which is devoted to normal infants, one to infected infants and the third to infants being prepared for removal to their homes.

So far as is practical, the hospital sends its small, electrically heated hand ambulance with an intern and nurse to bring the infant to the station. By so doing it avoids refrigeration, to a large extent, which is one of the chief causes of high mortality.

The equipment is simple, consisting of individual electrically heated water-jacketed beds, heated dressing tables, hygrometer, high and low temperature reading thermometer, quartz lamp and time clock.

Human milk is the diet used for all infants during the first days or weeks in the department, as their needs may indicate.

The station is under the care of a graduate nurse, who has under her direction the needed number of women trained for this special work, together with some nurses in training who may elect this special service.

In each instance, the mother is encouraged through the efforts of the social service department to keep up her supply of breast milk.

In preparation for return to their homes, the social service department visits the infants' homes at regular intervals for the purpose of instructing the mother in the preparation of feedings and the required hygienic care of the infants.

A special clinic for the graduated infants is conducted at the hospital for the ones who are likely to be neglected in their homes unless properly supervised. We believe that this later follow-up is to be ranked as of equal importance with the hospital care of the infant if good physical development is to be attained.

The station has had a steady growth since it was opened in 1922. During its first year, nineteen infants were received; in 1923, twenty-eight; in 1924, forty-seven; in 1925, sixty-six, and in 1926, 106. In our series of 266 cases, 138, or 51.9 per cent were discharged from the hospital, in most instances directly to their homes. Excluding the fifty-four infants who died in the first twenty-four hours, 66.9 per cent survived. Immaturity, refrigeration and neglect were the common causes of death in those dying in the first twenty-four hours.

Autopsies were performed in seventy-nine cases. Bronchopneumonia, with and without atelectasis, was present in a large number of the fatal cases. Intra-

cranial hemorrhage was found in thirty-one of the sixty-nine cases in which the skull was opened. Several other cases showed positive evidence of intracranial hemorrhage, which, however, was not proved by autopsy.

We have had no cases of cerebral hemorrhage without a history of cyanosis at some time or other.

During the past year Wassermann tests have been made on at least one parent of every infant admitted. During 1926, positive reactions did not average more than 10 per cent of all infants surviving more than twenty-four hours.

Multiple pregnancy (49 of 160 infants in the first year) was the most common single cause of premature labor. Many showed evidence of impaired vitality. Two of the forty-nine were from a triple pregnancy.

Approximately one seventh of the body weight of fluids and human milk of a food value of 70 calories per kilogram every twenty-four hours are required to maintain life. Little can be expected in the way of increase in weight until 90 calories are reached, and depending on the infants' weight, body surface and physiologic development, their later needs will approximate from 100 to 140 calories per kilogram of body weight. In exceptional cases, it may be necessary to feed breast milk in amounts equaling 160 to 200 calories per kilogram. Such infants are usually markedly underweight for their fetal age.

Other dietetic requirements are orange juice feeding which should be instituted by the third week, to counteract the effects of boiling and cod liver oil by the fourth week. To counteract the low iron content of these diets, egg yolk and carbonate of iron or citrate of iron and ammonia should be started by the fourth week. More recently, we have added yolk of raw egg to the breast milk to meet the iron requirement of the infants.

The infants are fed at the breast on leaving the station, when the mother has been able to keep her supply of milk. Complementary feedings may be necessary. Chymogen milk mixtures, or cultured lactic acid milk mixtures are used; these are usually started before the infants leave the station. Usually in the artificially fed, we have continued the Chymogen feedings throughout the first year. Some of the larger infants are changed to simple milk, water and sugar mixture before this time.

While many of the infants show minor, and a few moderate, degrees of rickets, only a small number have developed marked manifestations. We believe this to be due to the fact that cod liver oil and quartz light therapy were introduced when the infants were 2 or 3 weeks of age. We have had no cases of rickets requiring mechanical appliances or surgical intervention to correct deformities.

Megacephalus, while occasionally seen, disappears early, due, we think, to the early addition of cod liver oil to the diet together with daily exposure to the ultraviolet ray. Active signs of tetany did not develop in any of the infants of our series.

THE EARLY DIAGNOSIS OF BRONCHIECTASIS. DR. JEROME R. HEAD.

The introduction of iodized oil 40 per cent (lipiodol) as a contrast medium in roentgenoscopy of the bronchial tree has put the diagnosis of bronchiectasis on a new basis.

The oil is introduced directly into the trachea in amounts varying between 10 and 60 cc. and thence, by regulating the position of the patient, is made to flow by gravity into the portion of the lung that is under question. Roentgen-

ograms taken immediately after the administration show distinct shadows of the trachea, bronchi, the finer air passages, and any cavities that are connected with them.

There are a number of methods of making the injections — most of them simple and only slightly trying to the patient. In our experience the simplest, surest, most universally applicable and in many ways the least disagreeable is that by direct puncture of the cricothyroid membrane.

It is not difficult for the patients to restrain the cough during the injection and while the exposures are being made. Ten or twenty minutes later, most of them have a mild coughing spell during which most of the oil is expelled. This, however, is a more or less voluntary expulsion, and when the oil is used therapeutically in bronchiectasis the patients find no difficulty in retaining it for most of the day. That which enters the finer air spaces is not expelled by cough but remains in place and is gradually absorbed over a period of weeks or months. Injections have been made in many thousands of patients over a period of six years, and as yet no accidents or ill effects have been observed.

A series of approximately 100 patients whom we have recently examined are grouped according to the ages of onset and consultation as follows:

| Age | Onset | Consultation |
|---|---|---|
| From 1 to 5 years | 36 | 6 |
| From 1 to 10 years | 53 | 17 |
| From 11 to 20 years | 12 | 22 |
| From 21 to 30 years | 13 | 26 |
| From 31 to 40 years | 4 | 8 |
| From 41 to 50 years | 7 | 7 |
| From 51 to 60 years | 6 | 13 |
| From 61 to 70 years | .. | 2 |
| From 71 to 80 years | .. | 1 |
| 81 years | 1 | 1 |

The average duration before consultation was four years, the longest forty years and the shortest, six months.

These statistics demonstrate that bronchiectasis is primarily a disease of infancy and early childhood. The preponderance would be even more striking if one were to eliminate those cases which are secondary to more important conditions — bronchogenic carcinoma, aneurysm, and tuberculosis, diseases that account for many of the cases that occur in the later years of life.

The following classification presents in a relatively didactic manner the different causes of bronchiectasis in infants and children.

1. Congenital:
    1. A true error of development — Meyer.
    2. A type secondary to congenital atalectasis — Heller.
    3. A type secondary to syphilitic infection of the fetus — Balzer and Grandhomme.
2. Acquired:
    1. Secondary to acute bronchitis or bronchopneumonia.
    2. Secondary to obstruction of bronchus.
        *a.* Hilum glands.
        *b.* Foreign body.

Thirty-nine cases in which the onsets occurred before the eleventh year are grouped, according to etiology, as follows: pneumonia, 11; pertussis, 10; measles, 6; influenza, 1; foreign body, 3; sinusitis, 1; injury to back, 2; congenital, 4; total, 39.

Clinically, it is difficult to differentiate the cases according to etiology. Congenital bronchial dilatation frequently does not give symptoms until an acute respiratory infection, associated usually with one of the diseases of childhood, implants in the dilated tubes a chronic bronchitis; enlargement of the hilum glands is also frequently produced by an acute pulmonary infection; the respiratory symptoms secondary to unobserved aspiration of a foreign body are frequently mistaken for a simple pneumonia. Thus, these types of bronchiectasis are often confused with those truly caused by acute bronchitis, pertussis or pneumonia.

The true test of a new method of diagnosis is the help that it can give in the recognition of the early and atypical manifestations of disease. If it can clear up obscure cases and make possible earlier diagnoses, its value is inestimable. Diagnostic bronchography with iodized oil 40 per cent has done this for bronchiectasis, and consequently it seems probable that its greatest field of usefulness will be in the type of case described — in the early diagnosis of an obscure condition which, from a few symptoms and the possibility of recovery, progresses gradually to become one of the most distressing and incurable of diseases.

When bronchiectasis is once fully established and the sputum copious and continuous the only hope of cure is radical surgery. If the diagnosis were made early before repeated acute attacks had added to the injury, much might be accomplished by medicinal, postural and climatic treatment.

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*Regular Meeting, Feb. 15, 1927*

GEORGE E. BAXTER, M.D., *Presiding*

UROLOGY IN PEDIATRICS. DR. HERMAN L. KRETSCHMER (by invitation).

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

EXPERIMENTAL AND SPONTANEOUS PYELITIS IN THE RABBIT. DR. HENRY F. HELMHOLZ and MARIAN R. BOWERS.

In 1917, we isolated a strain of *Bacillus coli* from spontaneous pyelitis in a rabbit, which, when injected intravenously into rabbits, produced renal lesions in about 66 per cent of the animals injected. Intracystically injected, the bacillus produced infection in eleven of fifteen animals. Strains of colon bacilli isolated from pyelitis in infants and children had thus far failed to produce a large number of infections when injected into animals. Unfortunately, this colon bacillus with the specific localizing power was lost, and it was not until 1925 that we chanced on a colon bacillus, isolated from a case of pyelitis in a young infant, which produced renal lesions in nearly 100 per cent of the animals injected. This organism later lost its virulence, and it was another year before we again found another organism, this time from a rabbit suffering with spontaneous pyelitis, with the same specific localizing power. Thirty-one

of fifty-three animals injected with this bacillus developed renal lesions. Control injections of other strains of colon bacilli failed to produce infections of the urinary tract.

The outstanding feature of the experiments with intravenous injection was the development of cortical abscesses within twenty-four hours. These abscesses were about the size of a miliary tubercle, opaque, and sharply circumscribed. The abscesses seemed to work downward into the medulla, showing apparent infiltration toward the papilla. Although we have shown that pyelitis or inflammation of the pelvis can be produced by both intravenous and intracystic injection, little progress has been made toward a determination of the probable mode of infection.

In seventeen of twenty-one rabbits suffering with spontaneous bacilluria, cultures of the ureteral urine were sterile, although the urine from the bladder contained innumerable colon bacilli. In one instance, the urine from both ureters was found to contain innumerable colon bacilli; in the second, there were three colonies on the litmus lactose agar plate, but the culture in dextrose brain broth was negative; in the third, there were twelve colonies on the litmus lactose plate and the brain broth cultures were negative, and in the fourth, there were three colonies in the urine from the right kidney, and two in the urine from the left kidney, but these differed from the pure culture of *Bacillus coli* found in the urine from the bladder. It seemed probable that with one exception the ureteral urine was sterile and free from the organisms found in the bladder.

In considering the mode of infection, it seems probable that if these infections had been hematogenous, the organisms would have been found in the ureteral urine, as well as in that from the bladder, so that it is probable that the organisms reach the bladder by way of the urethra, thence by way of the ureters to the pelvis of the kidney.

DISCUSSION

Dr. C. A. Aldrich: I think the points in Dr. Kretschmer's paper are well taken. Judging from my small experience with cystoscopy in children, he is right in saying that this should be taken up with more enthusiasm. I think the only argument would be when cystoscopy should be performed, and I think this should be decided in each individual case. So many cases of pyelitis clear up within a few weeks in comparison with the numbers that continue and become chronic, that one should wait to see whether the case will clear up before he thinks of carrying out the more exact methods of diagnosis, just as Dr. Kretschmer has said.

I was interested in Dr. Helmholz's paper and his demonstration of the mechanism of ascending infection. To those of us who have always felt that there must be an ascending infection, on account of the preponderance of pyelitis in girls, it is gratifying to have it proved that this can occur.

Dr. Charles Schott: Dr. Kretschmer has probably done more and seen more of this work than all of us have together, and apparently his argument in picturing the symptoms and indications for his particular work proves that in these instances the child is a small adult. He has emphasized that the symptoms and picture in general are those of the adult, shown in the child. Pediatricians know that in most of their work they handle infants and children from their own particular point of view. The paper was interesting to me as Dr. Kretschmer gives me credit for starting him on this masterly work, but I think I do not deserve it. In certain cases, I thought that unquestionably there

were some pathologic changes in the urinary tract, but I know now that it was nothing but ammoniac ulcers on the glans penis. However, it is interesting to think that this work was started by such an error.

Dr. Helmholz's paper is beyond my discussion. The question of pyelitis stares one in the face all the time and is open to argument. It is known that girl babies have pyelitis more frequently and that the infection is ascending. The other causes, as he admits, are not positively proved.

DR. JOSEPH K. CALVIN: When Dr. Kretschmer reviewed the literature on urologic investigations in children, I do not think he gave himself enough credit. There was some investigation prior to 1923, but I believe his paper published in the *Journal of the American Medical Association* in that year stimulated more work than anything else had done. Since that time, the literature has been full of papers on urologic conditions in children. Pediatricians have been slow to follow along this line. I think one of the reasons is that urology in children is really a specialty within a specialty, and that urologists should realize that they are dealing with delicate tissues and with entirely different problems of specificity and immunity than in the adult. Just as some men are doing more surgery for children, probably some urologists are better equipped to treat urologic conditions in infants. In hospitals that are well equipped for children's operations, many more children are treated surgically than there would be otherwise. In hospitals that are not so well equipped for surgery, an attempt is made to treat the children medically for a longer period of time. I think the same thing holds true in urology, and until they are better equipped to handle such cases, the pediatricians are a little slow about referring them.

One type of case that Dr. Kretschmer did not touch on, namely, chronic hemorrhagic nephritis, I think for a time lends itself to urologic investigation. Two such cases were encountered in the clinic, with blood and casts in the urine. Tuberculosis, as well as stone and tumor, were fairly well ruled out, and on cystoscopic investigation it was found that the hemorrhagic urine was coming from one kidney. The condition was relieved considerably by decapsulation of the affected kidney. I think these patients should be subjected to urologic procedures at some time or other, especially if the condition is unilateral.

In regard to Dr. Helmholz's paper, one thing has always impressed me about pyelitis. The acute type seen in practice seems at times to be the result of upper respiratory infections. So often when the urine is examined, secondary pyelitis is found, but as a rule the organism is the colon bacillus. I wish Dr. Helmholz would tell us why the colon bacillus is the offending organism when the infection seems to be due to an upper respiratory infection.

DR. CLIFFORD G. GRULEE: I think the question is when the urologist should see the patient. That will vary with each individual patient. Dr. Kretschmer thinks that a large percentage of his patients were referred to him at a late date. I should say that they represented a definite conservatism which was more to be admired than otherwise. Many of the cases clear up within a few weeks or months following the usual line of treatment.

I have known of the work of Dr. Helmholz for some time, and no one can appreciate it more than I.

In looking up the age at which catheterization can be done, I found reports of one infant aged 29 days and one aged 3 days in which ureteral catheterization had been performed.

Dr. J. C. Spence, Newcastle, England: If anything practical has come to me out of the two papers, it is that this technic which the urologists propose to lend us will help the pediatrician to take more care in the clinical case, in which he can start fresh and make further study. He will not be confused with congenital anomalies and such things.

Dr. Helmholz has demonstrated that close histologic study of the specimens in the few fatal cases of pyelitis that occur will be of great assistance.

Dr. Joseph Brennemann: There is a sort of pediatric side to the question that should be emphasized, and that perhaps can be better done by someone whose memory goes back further than that of either of the essayists. I have been interested in pyuria for more than twenty years, because twenty years ago I had a little patient who had pyelitis and I did not know it. The parents decided to have a consultant, but he did not help us any. Dr. Abt was then called in and, being a little ahead of me on the literature, he examined the urine, which I had not done. It gave me a practical interest in pyuria in infancy. At that time and for some years afterward, we were interested in girl babies. Some time afterward Dr. Grulee had a case in a boy, which was a rare event. We naturally followed the idea that these cases were due to ascending infection. I wrote a paper some time later, in which I pointed out that these cases occurred in girl babies who still wore diapers and that they were due to ascending infection. I have never gotten away from that idea. I still believe that it is an ascending infection, but many cases of pyelitis of the old type are not seen now, doubtless because so little digestive disturbance exists among infants at present.

Pus is found frequently in the urine in cases of infection, chiefly infections of the upper respiratory tract, because they are the most common type encountered. The pyurias are just as frequent in boys as in girls, and in older children as in infants. These cases should not be called pyelitis but simply a pyuria complicating infection. I believe that there is an ascending infection that occurs practically only in girls, which is now rare, and that there is a pyuria which is a simple, transient thing of much more frequent occurrence, and which is seen in both the male and the female, and in which treatment is unnecessary, as it gets well as the original infection clears up.

I have been interested in the characteristic pathologic changes of hematogenous infection that Dr. Helmholz has pointed out before. I recently had a child with sepsis and a complicating pyuria, who came to necropsy, and the examination revealed the same cortical abscesses that Dr. Helmholz has described in the rabbit.

We know that Dr. Helmholz is giving us the latest information on this subject and that it is nearly all "home made." The negative information is just as valuable as the positive. If he did nothing more than demonstrate that there is a peculiar pathologic condition for the hematogenous infection and another pathologic condition for the ascending infection, and that there is such a thing as ascending infection, it would certainly be well worth while for him to have spent ten years on it. I think physicians are just becoming familiar with the fact that there are more patients that should be sent to the urologist than was once thought, and it is most valuable to have this brought home to us as clearly and forcibly as Dr. Kretschmer has done.

Dr. Julius H. Hess: Dr. Kretschmer spoke of two cases of hemorrhagic nephritis in his group. I recently have had a case that was under observation for about a year. The patient passed into the hands of Dr. Louis Schmidt

who reported that he could find no local causative factor. There was a history of tuberculosis in the mother. The girl died two weeks ago, at the age of 6, and the kidneys showed a high grade of secondary contraction, with little cortex. I mention this as a warning of the danger of coming to erroneous conclusions in protracted renal hemorrhage in children. This case was of especial interest because of the history of tuberculosis in the mother, which I had believed to be a factor in the child's case.

Dr. Louis W. Sauer: Pyelitis occurs in the newly born, and it has been my experience and I have found that it has also been the experience of Dr. Finkelstein that it is more common in boys. I wish to ask Dr. Helmholz whether he has had this experience in regard to the sexes.

Dr. Wilburt C. Davison, Baltimore: As most of the infants who suffer from pyelitis are girls, the natural assumption is that the infection is an ascending one, and I am delighted to find that Dr. Helmholz has some experimental proof that tends to support this general belief.

Dr. Kretschmer: Referring to the question of Dr. Aldrich as to when to perform cystoscopy in these children, it was answered when he said that each case is an individual one. I tried to bring out in the paper that cystoscopy was performed last and not first. After the infants are carried along for a reasonable time with the usual treatment and do not respond, I think one should try to find out why. It seems that if at the end of six months under good management the child still has pus in the urine, one is perfectly justified in investigating further.

Even if Dr. Schott did start us out via the ammoniac route, I feel indebted to him for starting me on this interesting problem.

I would like to have Dr. Calvin answer this question for me. He spoke of the children having upper respiratory infection and then of finding the colon bacillus in the urine. I should like to know how many children with infection of the upper respiratory tract have gastro-intestinal manifestations. It is easy to understand why they have pyelitis if there are gastro-intestinal symptoms. It is well known that gastro-intestinal symptoms are much more frequent during the summer. When histories have been taken in adults and an attempt has been made to elicit intestinal histories, it is not at all uncommon to get histories of persistent constipation, ulcers in the rectum, fissures in ano, etc. These patients have gastro-intestinal lesions that I believe allow the colon bacillus to filter out. If these children have gastro-intestinal complications, I think that explains why the colon bacillus is found so frequently.

Dr. Grulee raised the question about the time to bring in the children. I think they should be brought in early rather than late.

Dr. Helmholz raised the question of the route of the infection. I think his experiments show the routes. I believe there are many routes of infection. Some years ago at the Children's Hospital, work was done with normal infants without infectious disease or disease of the urinary tract. Their bladders were filled with thorium solution which would go up into the kidney, and pyelograms were obtained in this way. If it is possible for such a solution to travel up to the kidney via the ureter in normal infants, why is it not possible to have infected urine travel up into the kidney pelvis in the same way? In the cases of prostatic hypertrophy in men who strain when they urinate, and have chronic cystitis, I believe that they can carry up the infected urine in that way and have an ascending infection. Many of the women who are operated on for pelvic infections soon develop pus in the urine, a week later have pain in the

back and fever, and they must have an ascending infection. C. Francke was able to inject the lymphatics of the intestines, showing that they went up over the kidney on the right side and probably up to the kidney on the left side, demonstrating a direct lymphatic connection, so it is claimed, between the intestinal tract and the urinary tract. On this basis it is believed that some of the cases of infection by the colon bacillus have their origin in this way.

It seems to me that this subject is interesting, and the more one comes in contact with it the more interesting cases he sees and the more complex are the problems that are encountered.

DR. HELMHOLZ: I do not know why streptococcic infections of the upper respiratory tract are usually complicated by a colon bacillus pyelitis. About four years ago, I attempted to demonstrate that organisms obtained from infected tonsils that apparently were responsible for a pyelitis would tend to localize in the kidney, but I was unable to show such localization.

With regard to the relation of sex to pyelitis of the new-born, at present I have too few cases to permit conclusions that it is more common in boys than in girls. I believe that in these cases a bacillemia is being dealt with, and it is known that the colon bacillus frequently is found in the blood within the first few weeks of life.

I wish to emphasize that in the ascending infection only half of the cases studied showed periureteral polymorphonuclear infiltration of the lymphatics that ascended and involved the pelvic tissue. I am not referring to the lymphoid type of cells that occurs in almost any infection, but only to those cases in which the infiltration with the polymorphonuclear cell showed the eosinophilic granulations.

If pus is found in the urine of a patient suffering from a cold, it does not mean that the pus is coming from the bladder. There are many cases in which a clean looking vagina can add enough pus to the urine to make one think one is dealing with infection of the upper urinary tract. Until a series of cases, in which there have been catheterized specimens from girls or specimens collected from boys in the manner described by Dr. Kretschmer, have proved that these infections are of the bladder or of the upper urinary tract, I shall not feel that such infections are so frequent as is supposed.

I recently saw the niece of a doctor, who was supposed to have had a urinary infection for which she had been treated for two years. The child was about 40 pounds (18.1 Kg.) overweight. Examination of the vagina showed free pus, and examination of the urine proved it to be absolutely sterile. I know the men who say they are curing pyelitis in less than a week with 2 grains (0.13 Gm.) of sodium citrate three times a day are not treating pyelitis.

Dr. Kretschmer has done a great service in pointing out what the procedure should be in pyelitis. In acute pyelitis, definite obstruction is the one indication for surgical intervention. This group of patients should be catheterized. As a group, the majority of the cases are chronic, and the history must be studied and a culture made of the urine. Included in the examination there should be a roentgenogram of the kidneys, ureters and bladder, and a determination of the presence of residual urine. If all these examinations are negative, the child should receive thorough treatment with methenamine. I have had an unusual opportunity in the last six years to see chronic pyelitis as I never knew it in private practice. I have had cases that have persisted for four, five, and six or eight years, in which urologic examination should have been made years before. It is not easy to tell just when a child should be examined cystoscopically. I used to think I could tell this without the therapeutic test.

In one case a child had repeated attacks of fever up to 104 F., and colon bacilli and pus, grade 4, in the urine. The usual routine was gone through, as Dr. Kretschmer suggested, and the child had a cystoscopic examination at which the urine from both ureters was found to be sterile. The child had merely a cystitis, and on administration of methenamine in three days the urine was completely free from pus and bacteria.

Regarding the therapeutic use of methenamine, in a series of about a dozen cases that had persisted anywhere from one to three years I was able to cure the infection within a period of two weeks. The treatment probably will be considered somewhat drastic, and the dose necessary to sterilize the urine is likely to approximate closely the dose that will produce irritation in many individuals. If a beneficial effect is to be achieved, one shall have to approach the dose that will cause irritation of the urinary tract, but then he can stop. I use 15 grains (0.97 Gm.) of ammonium chloride and 7.5 grains (0.49 Gm.) of methenamine four times a day at six hour intervals. I then increase the dosage to 15 grains of methenamine four times a day, and even to 90 grains (5.85 Gm.) a day. One must see the patient every day and as soon as there is evidence of irritation, treatment must be stopped. If the methenamine is pushed to the point of irritation, I am sure that a large group of these cases, even if the infection had persisted for from two to six years, could be cleared up and would remain so without operative intervention. I have made it a rule in the chronic cases to treat the patient for at least two weeks with intensive methenamine therapy. If there is no result, I then insist on complete urologic examination. In this way a number of cystoscopic examinations have been avoided.

The field of chronic infections of the urinary tract requires close cooperation between the pediatrician and the urologist. In this way, a great many kidneys that at the present time are being destroyed by acute and chronic pyelonephritis can be preserved.

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## NORTHWESTERN PEDIATRIC SOCIETY

*Regular Meeting, Feb. 21, 1927, Minneapolis*

FREDERICK W. SCHLUTZ, M.D., *President*

MENTAL HYGIENE OF THE INFANT. DR. HYMAN S. LIPPMAN.

By teaching the child correct habits early in life, the chances for the development of undesirable traits are lessened. Formation of character should begin even earlier than the preschool age. It should begin in early infancy. Mental hygiene during this period must of necessity be directed to the parents and especially to the mother. The nervous, overanxious mother, filled with anxieties and a lack of confidence, leaves the hospital two weeks after she has given birth to an infant, and in addition to her new responsibility must care for the home. Much can be done for her mental health if these responsibilities are shifted for a few weeks. The obstetrician should have at his command a group of women who understand the handling of the mother and the infant and who can be used for such a purpose. More than anything else these women must be of a happy disposition, calm, and pleasant and free from a tendency to develop fears.

The average palatable diet can be made to contain all the ingredients necessary for the health of the mother and the promotion of an ample breast supply. It is not necessary to overstuff the mother with foods and liquids. This often results in the feeling of nausea and distress, and often of anorexia. In the case of the highstrung woman especially, it is advisable to have her remain on the diet to which she has been accustomed.

It is important that she should not become fatigued. She should sleep at least two hours every afternoon. Everything should be done to give her an uninterrupted night's sleep. Her responsibilities being cared for, she can get a certain amount of light exercise, preferably outdoors, every day.

The mother is exposed to too much literature. It is advisable that the obstetrician give her a good choice of reading matter. It is not advisable to wait until the pediatrician makes the selection.

The physician who cares for the nervous infant must know that it is to the detriment of the mother and infant if a rigid schedule is demanded. Hunger, thirst and restlessness in such an infant require more rapid relief. Cameron stresses the importance of feeding such an infant when he is quiet and relaxed, preferably when he is sleeping, even going so far as to give a grain of chloral by mouth to make him drowsy before placing him at the breast. Handling of this infant, other than by those who are in direct charge, should be done as little as possible. Noises and excitement of any kind should be eliminated. It is surprising that often after a few weeks of following a haphazard schedule, which may be necessary in the high strung infant, his nervous system becomes more stable, and he can be placed on a simple schedule and be content.

Such cases must be observed more closely, the observations tabulated more carefully, and statistics must be available to show that infants in the first two or three months are not as easily conditioned as one is led to believe.

Later in infancy problems tend to develop. Those that concern the mother most are finicky appetite, tantrums and thumb sucking. After all simple measure have failed, it has been found that ignoring the child will do more to eradicate these habits than any other one measure. Frequent visits and demonstrations from the nurse are necessary before even an intelligent mother can be taught to ignore the child. Once she has learned this, her problems begin to disappear. This is helped materially by finding playmates for the child and providing a playroom, in order to keep the mother from the child as much as possible. By so doing, the subtle pressures tend to be eliminated. The mother should know that symptoms of antagonism are signs of undue pressures and misunderstandings in management.

### DISCUSSION

DR. HELMHOLZ: The problem is so large that one can only discuss a small phase of it, and there is one thing that I should like to emphasize, and that is the question of discipline. The young child is going to want something from the parents every few minutes. It has always seemed to me that the logical time to break the demands on the parents is early in childhood. I think that the problems of the one who is with the child twenty-four hours of the day are entirely different from those of the one who is with him for only a few hours or a few minutes. I believe that with at least one, and in most cases, two or more children in his own home, the father gets an idea of what it means to live with a child. He will realize the state of the mother after fighting a long and losing battle.

DR. E. J. HUENEKENS: I agree with Dr. Helmholz in what he said about handling the child twenty-four hours of the day. A few of my patients did well in handling children as kindergarten teachers but have found the problem to be different with their own children. The Infant Welfare Society, realizing the problems of mental hygiene in infancy, has raised the age limit from 2 to 4 years. The parents receive such instruction at the clinics.

DR. EDITH BOYD: Go into the homes of these young mothers and see what they have gone through. After being in bed for ten days — in a wheel chair for a day — they are taken home. They send these girls out of the hospitals who have never seen an infant before, and expect them to give it the proper care. Some system should be worked out for the welfare of these girls.

DR. C. A. STEWART: The points enumerated in the paper are important. The advice given by the physician when he calls tends to soothe the mother. She has heard all kinds of advice, all conflicting, from her friends. If she has confidence in him a few words of advice go a long way.

DR. ADLER: It is wrong to call the infant a nervous child. Children vary just as all things vary. The infant, to begin with, is not nervous. The term complicates the situation.

DR. LIPPMAN: I agree with Dr. Adler that in speaking to the mother the doctor should not refer to the child as being "nervous." The fact must be faced, however, that a nervous infant as such does exist, evidenced by a general hypertonicity, abrupt jerky motor responses, and a tendency to vomiting, diarrhea and restlessness. The treatment of such an infant is different from that of an easy-going, phlegmatic one. Chloral and atropine are useful in the hypertonic, restless infant. Dr. Adler has stated that the nervousness of the hyperactive child is being exaggerated. Every effort should be made to emphasize to the mother that her problems are temporary and will clear up when the nervous system becomes more stable. I am glad Dr. Boyd emphasized the question of the mother leaving the hospital unprepared to care for herself or the child. I wonder if she has any suggestions to offer to remedy the situation when the mother is not able to afford extra help.

DR. BOYD: The only place that I know in which an attempt was being made to meet this problem was in San Francisco, where the visiting nurse was sent with the mother into her own home and the people paid only for the time that the nurse spent with them. For example, if the nurse was present only two hours each day, they paid her on that basis only. I think it would be for the good of the mother to have an exercise schedule arranged so that she will feel more physically fit on leaving the hospital.

MENTAL HYGIENE AND THE PRESCHOOL CHILD. DR. JOHN E. ANDERSON.

The importance of the home relations, of the individual and the importance of the early years of the child's life for later adjustment are being emphasized increasingly. For instance, hysteria, a complex mental disturbance of the adult period, seems to be the product of a long training of the individual, starting perhaps in infancy, to avoid difficult situations through the development of physical symptoms. In the adult period, that which started in the child as a reaction under control to a series of situations has become an automatic and thoroughly habitual response beyond the individual's control.

The pediatrician, with his close contact with the young child and the home, is in an exceptionally fortunate position to deal with potentially abnormal

traits near their inception, and to start both children and parents on the road to mental health.

Two generalizations are of considerable practical importance. The first of these is the emergence of what may be called an organismic conception of the individual, that is, the conception of the individual as a whole rather than in terms of particular organs, particular responses, or particular diseases. All aspects of the individual's life seem to be inextricably bound together. Nowhere is this seen more clearly than in the young child. What superficially seems to be a nutrition problem on further examination may be seen to be a sleeping problem or an emotional problem. What superficially appears to be a physicai problem may on further analysis be seen to be a mental problem, Similarly, a mental problem may reduce itself to a physical problem. Moreover, what at first glance seems to be purely a problem of the child, on further insight comes to be a problem involving the parents and home relations of the child.

The second principle concerns itself with the increasing emphasis in recent years on the fact that a study of the history of the individual is fully as important and in some cases more important than the study of the symptoms present at any one time. If the organismic conception is sound, it is obvious that the more one knows about the particular case, the better will be his handling of the situation. Frequently, facts that at first glance seem irrelevant become of fundamental importance in the light of the whole situation. The case history is a device for bringing large samples of the individual's behavior into view, as a supplement to the small sample seen in any one interview. In actual practice, however, as a man becomes more and more expert, he tends to devote less and less time to each case and to focus more and more on particular factors in the situation. Should not the expert, whatever his field, deliberately counteract this tendency by trying to take a larger view of the situation and move in the direction of a more complete study of each case? From the practical standpoint, the use of carefully worked out forms, filled out by the parent or by a nurse in consultation with the parent, can furnish much material to the expert who is forced because of pressure to devote less and less time to each case.

Much of our scientific training is in thinking of one variable as the cause of another. At all levels, behavior problems seem to be the product of a number of variables working together. For instance, the practical question as to whether spanking is or is not to be recommended as a disciplinary procedure cannot be settled dogmatically or by a single rule. In some situations, it may be valuable, in others harmful, depending on the other factors in the total situation. Workers in child welfare must, if they are to be successful in their attack on complex problems, learn to handle and analyze them in terms of a series of causes in complex relations.

The conclusion I should like to draw, and I think it applies equally well for both physical and mental hygiene, is that in order to treat the child effectively, one must know the physical and mental history, the home situation and the present condition, and above all, he must have a conception of a child as an organic whole. The cardinal principle is "Know the child."

DISCUSSION

DR. ROOD TAYLOR: Although I have heard many discussions of these problems, I have never heard one that put the matter so clearly. Dr. Anderson has hit at the fundamental principle in his emphasis on the knowledge of the whole child as the basis for efficient treatment.

DR. LIPPMAN: I would like to have Dr. Anderson tell a few of the things that are going on in the Institute of Child Welfare at the University of Minnesota.

DR. ANDERSON: The Institute of Child Welfare is an organization for the scientific study of the young child and for the dissemination of information about the child. It is interested primarily in the average or normal child, that is, the child that is found in the usual American home, rather than in the diseased, defective, or handicapped child. Many of its researches center about the study of the development of the child. The institute is carrying on investigations on infants, and on children between the ages of 2 and 5. It maintains a nursery school in which children are present from 9 a. m. to 4 p. m. and in which the children have lunch and afternoon naps. The members of the staff then are faced with eating and sleeping as well as other problems. Cooperating with the institute are a number of departments of the University: Anatomy, Pediatrics, Nervous and Mental Diseases, Psychology, Sociology, Education, Home Economics, and Public Health Nursing. The institute also gives instruction within the university and maintains an extension department which conducts study classes, carries on demonstrations, issues correspondence courses, and in other ways, seeks to bring information to the parents of young children.

DR. TAYLOR: Perhaps Dr. Anderson could give us the titles or brief descriptions of some of the researches now under way.

DR. ANDERSON: It is impossible to describe all our researches since we have about fifty specific projects going. In the field of anatomy, we are making studies of the growth of the body and its various parts by means of periodic measurements under the supervision of Dr. Scammon. We are also measuring the surface areas of children and checking them with basal metabolism. A study of posture is being made. A study of the development of the jaw and teeth with correlation of the results with the amount of thumb sucking is also being done. In the physiologic field, with the assistance of Dr. Schlutz, we are making studies of gastric contraction in infants, along with other projects. We are also preparing a bibliography of the literature on the physiology of the young child. In the psychologic field, last year we completed an extensive study of the validity of intelligence tests for young children and are this year developing on the basis of that study a more accurate measuring scale, with which we hope to tackle certain fundamental and practical problems in mental development. We are also conducting studies in language development, emotion, memory and learning. Studies are being made of eating and sleeping habits, and of the occurrence and control of anger responses. In the sociologic field, we are studying the relation between the child's reactions and his home and socio-economic status, and are carrying on special studies on the social reactions of children in their own groups. We are also making studies of the nutrition of children, and of the proper clothing for children. From these, which are only a few of the things under way, it can be seen how thoroughly we are touching every aspect of the child's life.

THE PRESCHOOL CHILD. DR. E. J. HUENEKENS.

The present system of education is overstressing the child's ego. Dr. Cameron, in his book "The Nervous Child," emphasizes that the signs of neuropathy

become more marked as the child grows older. Considering the relationships of the child to the school, one should emphasize the nursery school. In certain cases, this acts as a wonderful therapeutic weapon. For the only child, for the stimulated child, especially with an over-anxious mother, and the child who is smothered with attention, the nursery school functions to impress them with their unimportance. The kindergartens contribute their value not so much through their education as through their services as social centers. Dr. Blanton, is his book on child guidance, takes a reasonable stand in his discussion of handling the precocious child. I agree with him that, instead of advancing such a child too rapidly, when he would not be able physically and socially to compete with his fellow students, he should be given a greater number of tasks that would interest him, but would still keep him in the same grade. The Curtis speed tests are being generally used in the public schools in Minneapolis, and I feel that because of their deleterious effect on the shy, timid child, they should be discontinued. Their practical value is negligible. I should like to see the elimination of the driving type of teacher. The shy and typically nervous child suffers under such pressure. There is too much anxiety created in connection with his work. The driving teacher may be of value to a lazy St. Bernard type of child, but she is a detriment to the fox terrier type.

Educators are up in the air about the question of sex education in children. It seems that the more one studies about it, the less he knows. Such advice should come from the parents in a natural, chatty way. The child should not be left with the feeling that he is discussing a mysterious subject, to be referred to in whispers. As in any other problem, the personality of the child should determine the mode of attack. Sex facts should neither be hidden nor flaunted.

DISCUSSION

DR. ROOD TAYLOR: Dr. Huenekens' paper brings up some interesting facts. As a result of the efforts of the Women's Cooperative Alliance, who are teaching sex education to parents, the problems are becoming more complicated. Parents are more fearful and are probably more conscious of the subject than they should be. As regards the skipping of grades, I feel that the children lose the fundamentals of the work. There is a social problem to consider in the case of the girl at the age of 10 finding herself in a class of children from 12 to 14. I should like to see the school hours changed, and have the noon recess from 12 until 3, followed by the afternoon session.

DR. ADLER: I agree with Dr. Huenekens about the driving teacher. More problems result from such pressures than one realizes.

DR. LIPPMAN: Several years ago, Dr. Lashley sent questionnaires to the leading obstetricians and psychiatrists of this country to determine their stand on the question of sex education. Their opinions on the various phases of this problem varied so from one extreme to the other that he concluded that it would be impossible to formulate any system of sex education to meet with their approval. This may explain the confusion that must exist in the minds of the parents who are receiving sex instruction from a group that is attempting to

formulate laws without taking into account the personal equation of the parent and the child. Considerable work remains to be done on the study of sex, before any system of education can be advised. There are fewer driving teachers now than there were five years ago. There will be still fewer in the next five years. The Board of Education here and, I am sure, in other cities, is sponsoring child guidance work. They are cooperative and carry out the suggestions of psychiatrists.

# Book Reviews

THE TIRED CHILD. By MAX SEHAM and GRETE SEHAM. Pp. 329, with sixteen illustrations. Price, $2.00. Philadelphia: J. B. Lippincott Co., 1926.

This book is intended primarily for lay readers, and particularly for parents or for those having to do directly with the care of children. It might, however, be read with profit by all practicing physicians, especially by those dealing with children.

The subject of fatigue is well presented, and no one could read the book without being impressed with the importance of fatigue as an unfavorable influence in the life of children. Throughout the book the authors stress the individual child and, although the general principles are unenunciated, the application of these principles to the individual is clearly emphasized.

The definition of a normal child is ideal but probably is attained in every detail by few children.

The description of fatigue is clearcut; it portrays the picture vividly and is in sufficient detail to include all of its manifestations.

The diagnosis of fatigue by the questionnaire method is described in some detail and would undoubtedly be valuable in a study of some difficult individual children or if a group study was to be made of children in school.

The various factors that influence fatigue — teacher, parents, and family physician — are enumerated and discussed, together with a presentation of true stories of tired children. The necessity of proper habits of living in order to prevent fatigue is emphasized and is illustrated by actual cases. The part that the school, the teacher and the parent play in the arrangement of the necessary program and routine of the child implies the need of cooperative endeavor. It is questionable whether there is not some undue responsibility placed on the school with reference to the whole health problem in distinction to the relation of the parent and the family physician. Every parent might well read the chapter on what the parent can do to prevent fatigue.

The importance of considering the details of the child's daily life, sleep, rest, food, recreation and play are well presented.

The book contains an excellent bibliography.

COMMON PROCEDURES IN THE PRACTICE OF PEDIATRICS. By ALAN BROWN, M.D., and FREDERICK F. TISDALL, M.S., M.D. Pp. 259. Price, $4.00. Toronto: McClelland and Stewart, Ltd., 1926.

This book is simply what the name implies. It starts out with a description of history taking and physical examination followed by a chapter on infant feeding, which goes into the question more thoroughly than would be expected from the title of the book. The general ideas followed do not differ materially from those used in other places in this country and in Canada. This is followed by a chapter on the preschool and adolescent child. The first part of the chapter deals largely with diet and is practical, especially the various recipes and diet lists. The latter part of this long chapter, however, deals with formation of habits, and to the reviewer seems rather inappropriate in a book of this kind. It has, however, practical application for treating the child in the home. The chapter, "Diagnostic and Therapeutic Measures," is short.

The description of parenteral administration of fluids is complete and will be found extremely useful. "Special Procedures" takes up many of the things that have not been dealt with in other chapters, and then comes a description of the use of biologic products in the diagnosis and treatment of communicable diseases. This is especially practical and is well worth while. "Difficulties in Diagnosis" is of the same caliber but leaves much to be desired. "Laboratory Methods" is complete, while "Drugs" is as would be expected—short, and consists largely of a table of doses. Some tables are incorporated in the appendix. The book is not well written and in places the English is confused. On the whole, it is likely to prove of great benefit in the practical care and treatment of infants and children and can be recommended as a sane exposition of methods used in hospital care.

THE CAVITY SYNDROME IN THE TUBERCULOUS. By WALTER PIAGGIO GARZÓN. A monograph from the University of Montevideo, 1925. Pp. 150, with seventy-seven additional pages of roentgenograms.

The author's study of this condition is based on observations in 100 cases. He believes that the classic textbook descriptions do not really fit the actual clinical observations. The cavernous breathing, for example, always regarded as a major and constant symptom, is not always present. In spite of definite and proved formation of cavities it may be absent. Typical cavernous blowing respiration was present in only about 50 per cent of the cases. On the other hand, various moist râles are always present and are the most constant physical observation in the cavity. They have great semiologic value on account of the peculiarity of pitch and note. The peculiar modifications of the transmitted voice on combined auscultation and percussion and the vocal fremitus and additional signs aid in definitely locating cavities. They are by no means constantly present.

The author attaches great importance to the counting of Cushman's spirals in the sputum and regards their presence and the proper evaluation of the physical signs of the various râles on auscultation as the most certain and definite evidences of the formation of cavities.

The author does not agree with the statement of some observers that the formation of cavities commonly is characterized by absence of physical signs. He particularly challenges the statement that auscultatory signs are absent in more than 50 per cent of the cases.

The monograph contains a series of exceptionally fine roentgenograms showing the formation of cavities in various stages and also a series of sketches and drawings.

The author believes that injections of iodized oil 40 per cent have only a limited use in establishing the diagnosis of pulmonary cavities and are generally contraindicated.

DIRECTORY OF RESEARCH IN CHILD DEVELOPMENT NUMBER 76. By LESLIE RAY MARSTON. Pp. 38. Price, 50 cents. National Research Council, Washington, D. C., 1927.

This is a valuable directory, containing the names of those who are doing work in child development, together with the subjects on which they are working. It will be found of value to any one who wishes to get in touch with such work.

# Directory of Pediatric Societies

## NATIONAL

### AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: To be decided later.

### AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

### THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: Spring.

### AMERICAN CHILD HEALTH ASSOCIATION

President: Mr. Herbert Hoover, Department of Commerce, Washington, D. C.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

### CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Howard Spohn, 718 Granville St., Vancouver, B. C.
Secretary: Dr. Frederick F. Tisdall, 102 College St., Toronto, Ont.

## SECTIONAL

### CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. O. L. Goehle, 15703 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. H. T. Price, 121 University Place, Pittsburgh.
Place: Cleveland. Time: Oct. 14 and 15, 1927.

### SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

President: Dr. Robert A. Strong, Pass Christian, Miss.
Secretary: Dr. Hugh L. Dwyer, Medical Arts Bldg., Kansas City, Mo.
Place: Memphis, Tenn. Time: Nov. 14 to 17, 1927.

**LOCAL**

### PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Pl., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from September to April, at 8 p. m.

### BROOKLYN PEDIATRIC SOCIETY

President: Dr Harold L. Barnes, 1235 Dean St., Brooklyn.
Secretary: Dr. Charles A. Weymuller, 96 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

### CHICAGO PEDIATRIC SOCIETY

President: Dr. George Baxter, 4603 Broadway, Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

### THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. Henry J. Gerstenberger, 2103 Adelbert Road, Cleveland.
Secretary: Dr. Charles W. Burhans, Lakeside Hospital, Cleveland.
Place: 2009 Adelbert Road. Time: Feb. 10, May 7, Sept. 22 and Dec. 15.

### DETROIT PEDIATRIC SOCIETY

President: Dr. Thomas B. Cooley, 987 Jefferson Avenue, East, Detroit.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

### LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.
Place: New Orleans. Time: April 25, 1927.

### MEMPHIS PEDIATRIC SOCIETY

President: Dr. Walter L. Rucks, 1074 Madison Ave., Memphis, Tenn.
Secretary: Dr. J. B. Blue, Columbian Mutual Tower, Memphis, Tenn.
Place: Baptist Memorial Hospital. Time: Second Tuesday of each month.

### MILWAUKEE PEDIATRIC SOCIETY

President: Dr. Roy M. Greenthal, 141 East Wisconsin Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month.

## NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

## PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

Chairman: Dr. Lewis C. Schroeder, 39 E. 61st St., New York.
Secretary: Dr. William R. May, 8 East 66th St., New York.
Place: New York Academy of Medicine. Time: Second Thursday of each month.

## NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. C. F. Gelston, 384 Post St., San Francisco.
Secretary: Dr. Mary H. Layman, 2116 Pacific Ave., San Francisco.
Place: Alternates between Stanford University Hospital, University of California Hospital, and Children's Hospital. Time: Three or four times a season.

## NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. C. A. Stewart, 730 La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: Three at the Medical Campus, Minneapolis and one at the Town and County Club. Time: Winter, Spring, Summer, Fall.

## PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Frederick Fraley (Retiring), Overbrook, Pa.
Secretary: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month.

## THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, Republic Bldg., Denver.
Time: Third Saturday of each month, 2 to 4 p. m. Place: Children's Hospital, Denver.

## ST. LOUIS PEDIATRIC SOCIETY

President: Dr. T. Wistor White, Lister Bldg., St. Louis.
Secretary: Dr. Edwin Rohlfing, Grand Blvd. and Wyoming St., St. Louis.
Place: St. Louis Children's Hospital. Time: Third Friday in each month.

## SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Joseph Shuman, 1136 West 6th St., Los Angeles.
Secretary: Dr. Wm. Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

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